THE REACTION OF DINITROGEN TETROXIDE WITH UNSATURATED HYDROCARBONS

A Thesis

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Doctor of Philosophy

in the

University of Glasgow

by

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Chemistry Department September 1957

PREFACE

It is with much pleasure that I thank Dr. J.C.D. Brand, under whose supervision this work was carried out, for much helpful discussion and invaluable advice. The micro-analyses recorded herein were determined by Mr. J.M.L. Cameron and his staff, for which I am most grateful. I would also like to thank Miss A.W.P. Jarvie for carrying out the deuterium estimation.

This work was carried out partly during the tenure of a James Fleming Scholarship, for which I am indebted to the University of Glasgow, and partly while I was in receipt of a Carnegie Senior Scholarship, for which I cordially thank the Board of Trustees of the Carnegie Trust for the Universities of Scotland.

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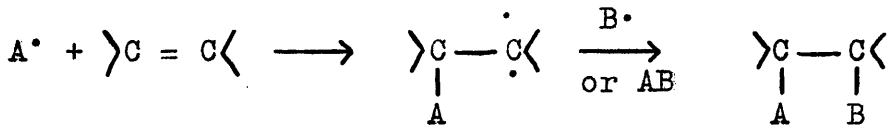
INTRODUCTION

Introduction

Although it had been established by 1937 that the heterolytic addition of species such as the halogens and hypohalites to carbon-carbon double-bonds proceeds in a stereospecific manner, so that the entering groups are trans to each other,[6,59] no work on the stereochemistry of homolytic addition reactions has been done until comparatively recently. An a priori consideration of such a reaction leads one to the conclusion that the stereochemistry of the addition process will depend on the spatial configuration of the intermediate radical I.



I

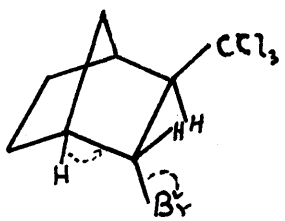
The evidence concerning the stereochemistry of a free-radical has recently been reviewed by Hine,[39] and from it one can draw the conclusion that a free-radical is either planar, like a carbonium ion, or else is pyramidal with a rapid inversion, comparable to ammonia. On this basis, one would expect the addition reaction to be non-

stereospecific, unless some special effect, such as the formation of a non-classical radical, were operating.

The first evidence of any note on the stereochemistry of homolytic addition reactions was published by Mayo and Wilzbach in 1949[50]. They reported that the same product was obtained from either cis or trans dichloroethylene in co-polymerisations with vinyl acetate. The identity was based on the identical rates of dehalogenation of the polymers with iodide ion. They therefore suggested that the radical produced in the chain propagation step viz:- R.CHCL.$\dot{C}$HCL equilibrates by rotation or inversion among its possible conformations more rapidly than it adds to another monomer unit.

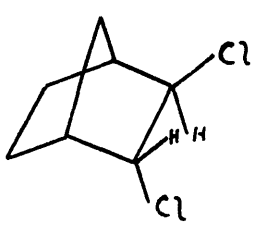
In the same year, Kharasch and Friedlander published the results of an investigation into the free-radical addition of bromotrichloromethane to a large number of olefins[43]. They made no specific observations on the stereochemistry of the process; but in a review the following year, Fawcett[28] interpreted their results on the ease and direction of dehydrohalogenation as being indicative of trans addition. His argument was based on the preferred trans elimination of hydrogen bromide with alkali, and the fact that there was no elimination

from the adduct of bromotrichloromethane and bicyclo [2:2:1] heptene. If the addition had been trans, one would expect a product like II, in which trans elimination of hydrogen bromide would involve a violation of Bredt's rule.



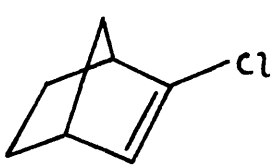
II

However, Roberts and his colleagues[60] have shown that the base catalysed elimination of hydrogen chloride from trans-2:3-dichlorobicyclo[2:2:1]-heptane (III) to give 2-chlorobicyclo[2:2:1]heptene (V) occurs more readily than from cis-endo-2:3-dichlorobicyclo[2:2:1]-heptane (IV), which throws considerable doubt on the validity of Fawcett's argument.

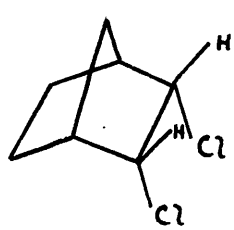


trans

III



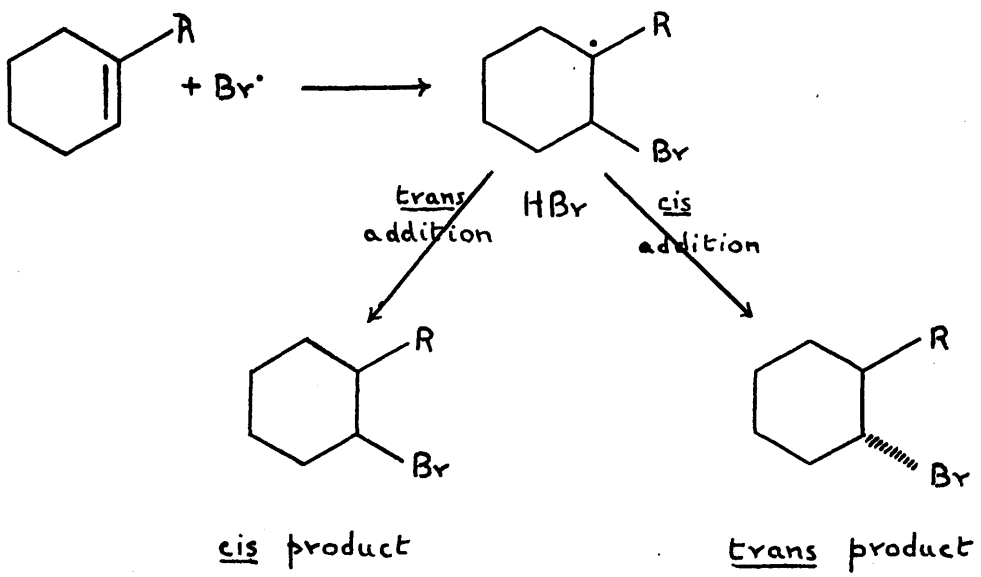
V



cis

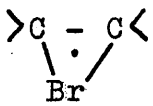
IV

In 1952, however, Goering, Abell and Aycock showed that the free-radical addition of hydrogen bromide to 1-bromo and 1-methylcyclohexene gave, as sole product, the cyclohexane derivative with the two substituents cis to each other[32], indicating that stereospecifically trans addition had taken place. Goering assumed that the product is the thermodynamically less stable isomer, and hence that the possibility of cis addition followed by a trans to cis isomerisation is precluded.

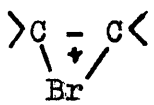


In order to account for the stereospecificity, Goering and his co-workers suggested that a 3-membered radical ring VI, comparable to the halonium ion ring of heterolytic

addition VII, maintained the stereochemical integrity of the intermediate, forcing the consummating hydrogen to enter <u>trans</u> to the initial bromine.

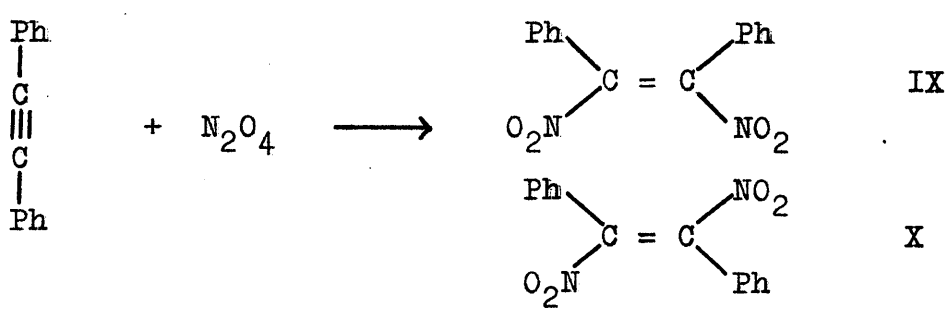


VI



VII

The following year Campbell, Shavel and Campbell reported that the addition of dinitrogen tetroxide to diphenylacetylene VIII gave a mixture of <u>cis</u> and <u>trans</u> dinitrostilbenes (IX and X)[20].



IX

X

At the time they used the evidence of non-stereospecificity tentatively to suggest that the addition of dinitrogen tetroxide was a radical process, because, although not as well studied as olefins, ionic addition

to acetylenes is almost certainly trans[57,65]. As will be shown later, the reaction of dinitrogen tetroxide with carbon-carbon multiple bonds is indeed a free-radical one.

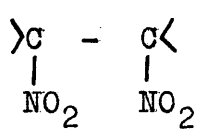
Recently the free-radical addition reactions of olefinic systems have been extensively reviewed by Cadogan and Hey[19] and their review shows that while a considerable amount of work has been done on these reactions, only a very little of it has been concerned with the stereochemistry of the process.

Thus when this work was commenced, in 1954, there were, apart from theoretical considerations, these few conflicting pieces of evidence on the stereochemistry of radical addition. The object of the work was to determine the mechanism of the reaction of dinitrogen tetroxide with olefins and to examine the stereochemistry of the process.

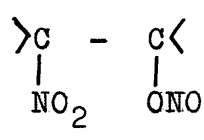
Mechanism of the Addition of Dinitrogen Tetroxide

Previous Work

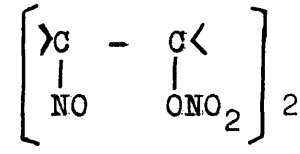
The reaction of dinitrogen tetroxide with organic compounds was reviewed by Riebsomer in 1945[58], and an analysis of the additions to olefins that he reports shows that three main modes of addition take place viz:-



XI



XII

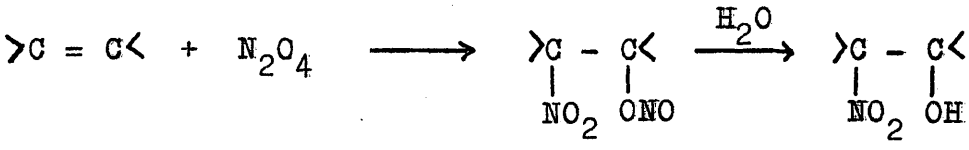


XIII

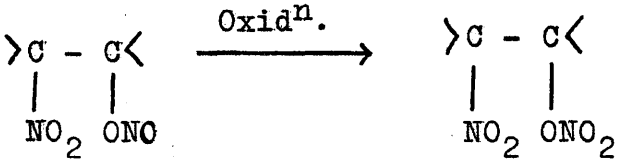
As Riebsomer points out, however, much of the work was carried out with 'nitrous fumes,' a reagent consisting of dinitrogen trioxide and tetroxide in uncertain amounts, and much reliance can not be placed on it. In fact the work of Levy and his collaborators has shown that the third mode of addition (XIII) is due to addition of dinitrogen trioxide as NO and ONO followed by oxidation of nitrite to nitrate[49a].

Levy and his associates placed the addition reaction of dinitrogen tetroxide to olefins on a firm experimental basis between 1946 and 1949[49a-e], and showed that two

main products were obtained, dinitro compounds (XI) and nitro-alcohols (XIV), which were formed by hydrolysis of the nitrite esters (XII). Small quantities of nitrate esters (XV) were also formed by oxidation.



XII XIV



XV

Levy stressed the necessity for using pure tetroxide and peroxide-free olefins to obtain consistent results and stable products. The work of Levy and his colleagues, which was confined to alkenes has been extended to a wide variety of other olefins by the work of Porter and Wood[55], Weghofer[80] and Vil'yams and Vasil'ev[78,77] and to acetylenes by Campbell and his co-workers[20] and by Freeman and Emmons[30].

At the time Levy's work was carried out, interest in the chemistry of the nitronium ion stimulated Levy[49a], in conjunction with Ingold[40], to postulate an ionic mechanism for the reaction. They postulated that the tetroxide first heterolysed, with subsequent attack by

$$N_2O_4 \rightleftharpoons NO_2^+ + NO_2^-$$

the nitronium ion.

$$\rangle C = C\langle + NO_2^+ \longrightarrow \rangle \underset{\displaystyle NO_2}{\overset{\displaystyle |}{C}} - \overset{+}{C}\langle \longrightarrow \text{PRODUCTS}$$

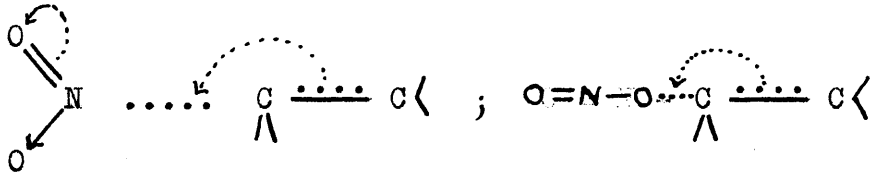
(or equivalent non-classical form)

This hypothesis satisfactorily explained the observed orientation i.e. the initial attack was at the carbon carrying more hydrogen, and was accompanied by carbon to nitrogen bond formation. However, it has been shown that under heterolytic conditions dinitrogen tetroxide ionises to give a nitrosonium ion and nitrate anion[1,36],

$$N_2O_4 \rightleftharpoons NO^+ + NO_3^-$$

an ionisation which does not explain the observed

products. Further, dinitrogen tetroxide is known from paramagnetic and spectral studies to homolyse readily to nitrogen dioxide radicals[36], and a free-radical mechanism also explains the orientation observed. Initial carbon to nitrogen bond formation is not so readily explained, but it can be done on the basis of the greater hyperconjugative resonance in the transition state which accompanies carbon to nitrogen XVI rather than carbon to oxygen XVII bond formation.



XVI XVII

Fresh evidence in favour of a homolytic mechanism was provided in 1953 by the work of Schechter and Conrad on the orientation of the addition of dinitrogen tetroxide to methyl acrylate[63]. Their results are summarised below.

$$N_2O_4 + H_2C = CH.CO_2Me \longrightarrow \begin{cases} O_2N.CH = C.CO_2Me & (13\%) \\ O_2N.CH_2 - CHOH.CO_2Me & (27\%) \\ \text{Oxalic acid} \\ \text{Nitrogen containing polymers} \end{cases}$$

They found no evidence for the formation of any product in which a nitrite group had become attached to the β-carbon atom of the acrylate, in spite of a careful search. Now, if the addition reaction had proceeded by an ionic mechanism, one would expect as products

$$H_2C^{\delta+}=CH^{\delta-} \longrightarrow CO_2Me + NO_2^+ \longrightarrow H_2C^+ - \underset{NO_2}{CH}.CO_2Me$$

$$H_2C^+.CH(NO_2).CO_2Me + NO_2^- \longrightarrow \begin{cases} ONO.CH_2.CH(NO_2).CO_2Me \\ O_2N.CH_2.CH(NO_2).CO_2Me \end{cases}$$

whereas a homolytic mechanism would predict

$$H_2C = CH.CO_2Me + \dot{N}O_2 \longrightarrow O_2N.CH_2.\dot{C}H.CO_2Me$$

$$O_2N.CH_2.CH.CO_2Me + \dot{N}O_2 \longrightarrow \begin{cases} O_2N.CH_2.CH(ONO).CO_2Me \\ O_2N.CH_2.CH(NO_2).CO_2Me \end{cases}$$

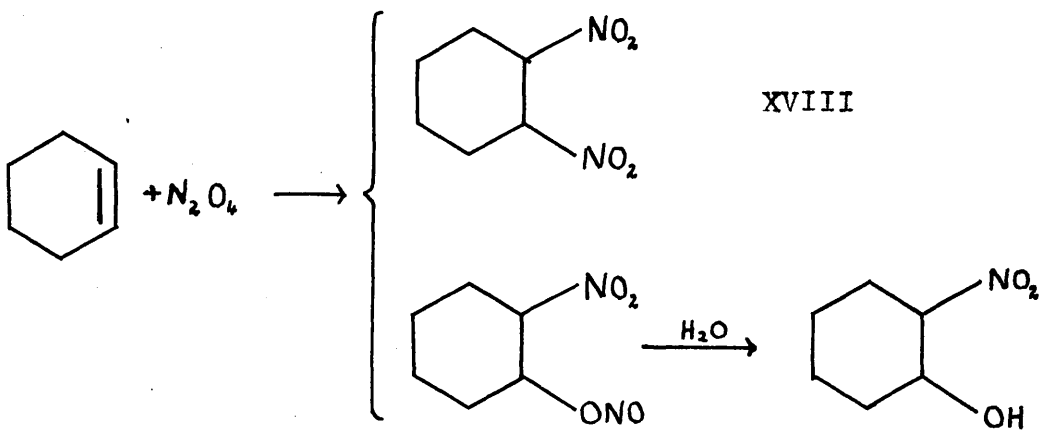
That the observed orientation is in the same direction as for simple olefins (i.e. those with no polar substituents), and in the opposite sense to that predicted by an ionic mechanism, led Schechter to suggest that the reaction "may occur essentially by a homolytic process." A conclusion supported by the occurrence of polymerisation products, albeit not well characterised.

The Effect of Bromotrichloromethane on the Reaction

With the above evidence in mind, it is fairly obvious that a conclusive demonstration of the free-radical nature of the reaction can be achieved if a reagent known to be specifically active towards free-radicals diverts the course of the reaction when it is present in the reaction mixture. That this might occur can be inferred both from Levy's observation that, in halo-carbon solvents, considerable "oxidation" took place[49a], and from the results of Baryshnikova and Titov[8], who found that when the addition of dinitrogen tetroxide to cyclohexene was conducted in bromoform solution, the (unidentified) product contained appreciable quantities of bromine.

The reaction of dinitrogen tetroxide with cyclohexene was therefore carried out in the presence of bromo-trichloromethane, a suitable radical transfer agent.

Levy and his co-workers have shown that the addition of dinitrogen tetroxide to cyclohexene in ether solution gives almost equimolecular amounts of 1:2-dinitrocyclohexane XVIII and 2-nitrocyclohexanol XX produced from the nitrite XIX by hydrolysis during working-up[49e].



XVIII

XIX XX

The reaction was carried out by distilling the dinitrogen tetroxide in a stream of oxygen into a solution of 3 equivalents of cyclohexene and 10 equivalents of bromotrichloromethane in ether at 0°C. The products isolated from the reaction, and their respective yields (expressed as molar percentages of the total yield) are given in Table I.

TABLE I

Compound		Yield
2-bromo-1-nitrocyclohexane	XXI	30.1
1-bromo-2-chlorocyclohexane	XXIII	32.0
2-chlorocyclohexanol	XXV	28.0
2-Chlorocyclohexyl nitrate	XXVI	4.2
trichloronitromethane	XXII	1.6
cyclohexene nitrosite		0.9
1-nitrocyclohexene	XXVII	3.3
nitrosyl chloride, phosgene		Traces

Total yield on dinitrogen tetroxide or cyclohexene ca 65%.

The analysis of the reaction mixture was carried out mainly by infra-red spectrometric methods. The reaction mixture was readily fractionated into three portions. The volatile components were removed in the falling-film evaporator during working up; and the residual oil gave, on distillation, two fractions. The lower boiling was a mixture of 1-bromo-2-chlorocyclohexane XXIII and 2-chlorocyclohexanol XXV, and the higher boiling was a mixture of 2-bromo-1-nitrocyclohexane XXI, 2-chlorocyclohexyl nitrate XXVI,

1-nitrocyclohexene XXVII and a small amount of 1-bromo-2-chlorocyclohexane XXIII. Tables II and III give the infra-red spectra of these mixtures and those of the pure components.

The nature and diversity of the products isolated shows that considerable interaction with the bromotrichloromethane took place. Since bromotrichloromethane is inert to nitrogen dioxide, and since light was excluded, these results can only be explained if the bromotrichloromethane were acting as a radical transfer agent. It will be noticed that neither of the 'normal' products of the reaction was detected, although a careful search was made. showing that even if the reaction took place partly by a radical, and partly by an ionic process, the ionic reaction is of insignificant proportions. The possibility of a rapid radical chain reaction can be excluded because of the large number of chain terminators which are present. The reaction of dinitrogen tetroxide with olefins therefore occurs by initial homolysis,

$$N_2O_4 \rightleftharpoons 2\ NO_2^{\cdot}$$

followed by association of a nitrogen dioxide radical with olefin.

TABLE II

Mixture	XXIII	XXV	Assignment*
3530 w.		3540 m.	XXV
3410		3358	XXV
1448 m.s.	1444 m.s.	1448 m.s.	CH_2 deformation
1362 w.	1356 v.w.	1362 w.	
1342 w.	1340 w.	1334 v.w.	
1279 w.	1277 w.		XXIII
1264 w.		1264 w.	XXV
1215 v.w.	1214 v.w.	1215 m.	
1184 m.	1184 m.s.		XXIII
1122 v.w.	1132;1118 w.	1128 w.	
1080 m.		1079† s.	XXV
1038 v.w.	1035 v.w.	1042 w.	
1004 w.	1002 m.		XXIII
978 w.	976 m.	980 v.w.	
960 m.		960 s.	XXV
905 w.	905 m.s.	906 v.w.	mainly XXIII
		894 v.w.	
862 w.	861 m.	864 m.	
842 w.	841 m.	843 w.	mainly XXIII
816 w.	815 m.		XXIII
797 w.		797 m.	XXV
741 m.	741 m.		
734		735 m.s.	
694 m.	693† m.s.		XXIII
658 w.	658 w.		XXIII

* Where there is no assignment, the band is common to both compounds.

Key. m.s. = a little stronger than medium strength band.
m. = medium strength band.
w. = weak.
v.w. = very weak.

Bands marked † were used for quantitative analysis.

TABLE III

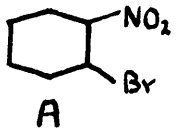
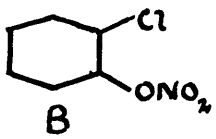
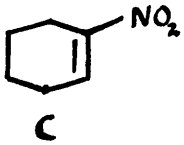
Mixture	 A	 B	 C	Assignment
1637 s.		1633† v.s.	1670 w.	B + C
1557 v.s.	1553† v.s.			A
1520 m.			1520† v.s.	C
1450 m.s.	1450 m.s.	1450 m.s.	1450 m.	Common
1374 s.	1372 s.		1438	A
1353 (sh.)	1350 m.			A
1346 m.			1344 v.s.	C
1336 m.	1332 m.	1338 w.	1340	Common
1326 (sh.)		1324 m.		B
1296 (sh.)	1296 m.			A
1280 s.		1278 v.s.		B
	1266 w.			
1244 w.	1238 w.			A
1220 v.w.	1220 v.w.	1220 w.		A + B
1206 v.w.	1206 v.w.	1206 w.		A + B
1192 m.	1190 m.			A
1130 v.w.	1125 w.			A
1188 v.w.				XXIII
1108 w.	1107 m.			A
1084 v.w.			1084 w.	C
1062 w.	1063 v.w.		1062 m.	C + A
	1048 v.w.	1050 v.w.		A + B
1007 w.		1012 m.		B
994 (sh.)	994 m.			A
	954 w.			
946 w.		949 m.		B
923 w.	925 m.		930 m.	A + C
913 (sh.)		914 w.		B
899 m.	898 m.	894 (sh.)		A + B
872 m.s.		874 s.		B

TABLE III (contd.)

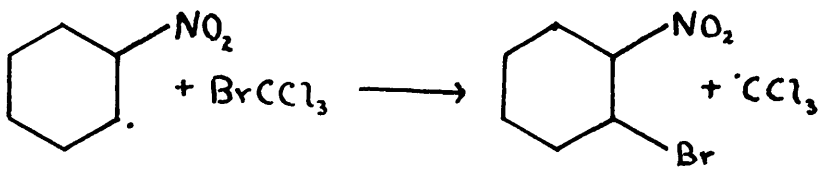
Mixture	A	B	C	Assignment
855 m.		857 s.		B
848 (sh.)	848 m.			A
843 (sh.)		844 s.		B
823 w.		819 v.w.	823 m.	C + B
807 w.	807 m.	808 w.		A + B
802 (sh.)			800 w.	C
757 m.				NOT IDENTIFIED
748 m.		747 m.		B
736 m.	736 v.s.		737 m.	A + C
		713 w.		
696 m.	697 v.s.	696 m.	696 m.	Common
670 w.				

Key. v.s. = very strong band
s. = strong band
(sh.)= shoulder
see also Table II.

1.

In the presence of bromotrichloromethane this radical abstracts a bromine atom

2.



XXI

giving 2-bromo-1-nitrocyclohexane XXI and a trichloromethyl radical. Now trichloromethyl radicals are known to react with olefins[19], and since no products of such a reaction are found, the trichloromethyl radical must undergo some other more rapid reaction. This is apparently combination with a nitrogen dioxide radical,

3.

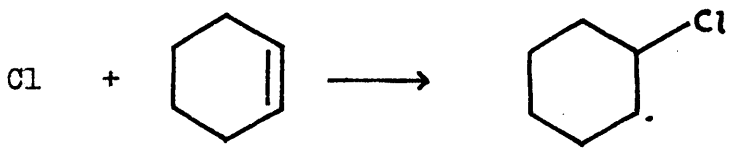
$$\cdot CCl_3 + NO_2^{\cdot} \longrightarrow \begin{cases} CCl_3NO_2 & \text{XXII} \\ CCl_3O^{\cdot} + NO^{\cdot} \end{cases}$$

to give trichloronitromethane XXII, one of the isolated products, and a trichloromethoxy radical, possibly

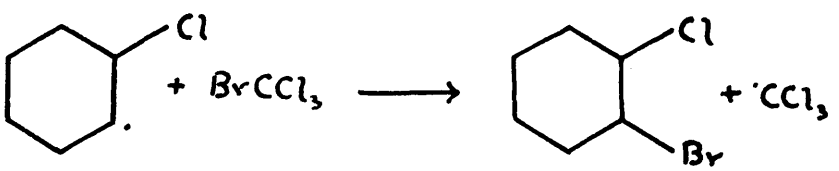
through the transitory intermediate of trichloromethyl nitrite[36]. The trichloromethoxy radical then decomposes giving phosgene and a chlorine atom.

4. $CCl_3O^{\cdot} \longrightarrow COCl_2 + Cl^{\cdot}$

The chlorine atom combines with olefin to give a chlorocyclohexyl radical, which can react in either of two ways.

5. 

The first is with a bromotrichloromethane molecule,

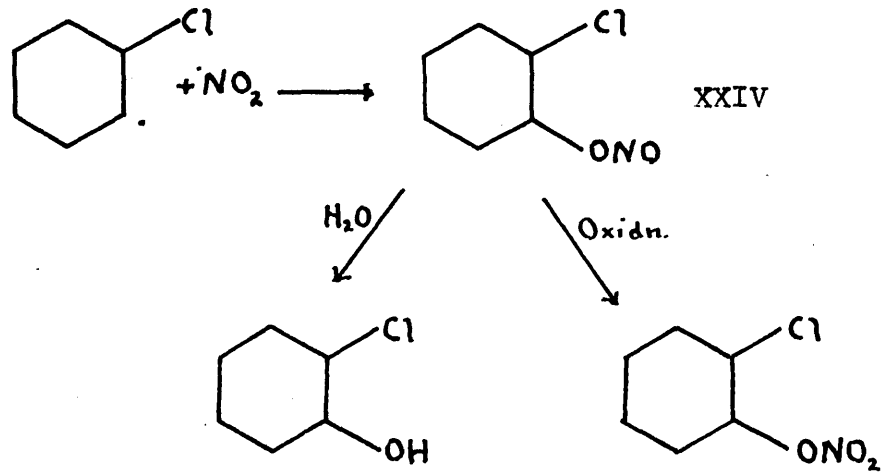
6. 

XXIII

to give 1-bromo-2-chlorocyclohexane XXIII and another trichloromethyl radical, thus completing a cycle. The second is by reaction with nitrogen dioxide to

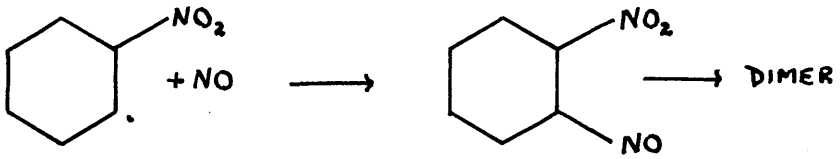
give 2-chlorocyclohexyl nitrite XXIV,

7.

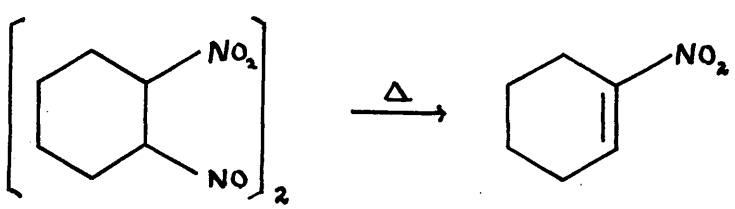


XXV XXVI

which is either hydrolysed during working up to 2-chlorocyclohexanol XXV or oxidised during the reaction to the corresponding nitrate XXVI. The reactions 3, 4, 5 and 6 form a cycle which is self-supporting, while 7. forms a termination step. Since the chlorobromide XXIII and the alcohol XXV, or its ester XXVI, are formed in approximately equal amounts, this cycle is apparently only completed once before termination. As the concentration of nitric oxide, from reaction 3 increases, towards the end of the reaction, reactions such as

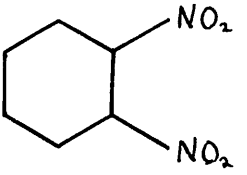
8. 

presumably come into play giving cyclohexene nitrosite. Reaction 8 can only form a termination step, since Brown has shown that nitric oxide does not attack olefins at room temperature[16]. The formation of 1-nitrocyclohexene XXVII may be explained by loss of hydrogen from a nitrocyclohexyl radical, but it is much more likely that it arises by pyrolysis of nitrosite during the latter stages of the distillation, since the nitrosite is quite soluble in the mixture of nitro- and chloro-compounds formed by the reaction.

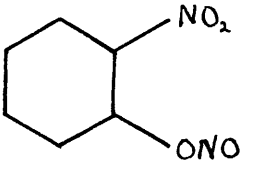


XXVII

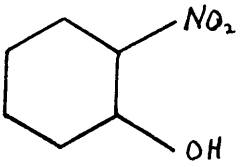
Formula Sheet for Chapter 1.



XVIII



XIX



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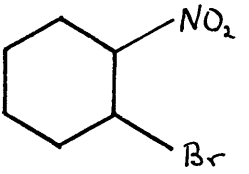
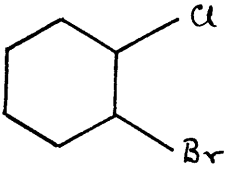


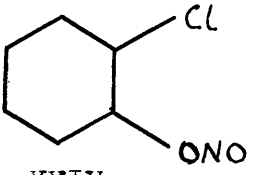
XXI

CCl_3NO_2

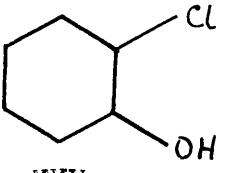
XXII



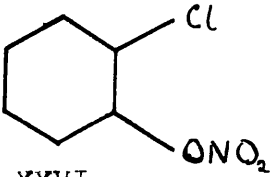
XXIII



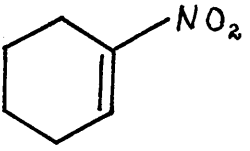
XXIV



XXV



XXVI



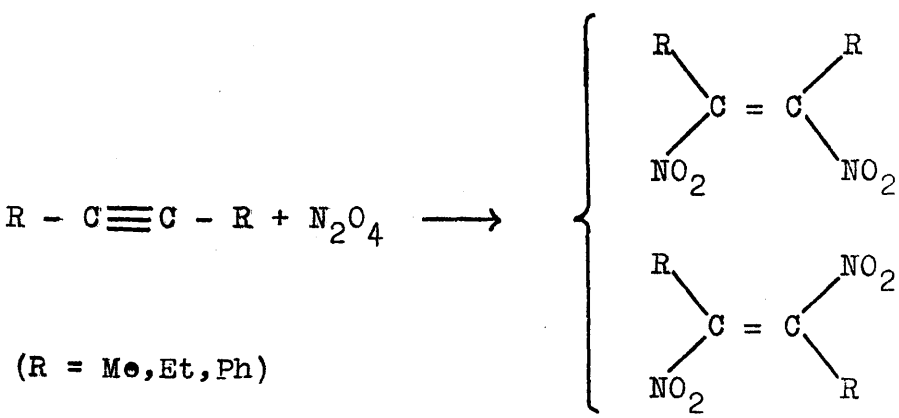
XXVII

CHAPTER 2

The Stereochemistry of the Addition of Dinitrogen Tetroxide

Stereochemistry of the Addition of Dinitrogen Tetroxide

Although many references to the addition of dinitrogen tetroxide to unsaturated systems are to be found in the chemical literature, none gives any indication of the stereochemistry of the products except for that of Campbell and his colleagues[20], which was mentioned in the introduction, and very recently a paper by Freeman and Emmons[30]. They too had reacted dinitrogen tetroxide with acetylenes and had found that a mixture of stereoisomeric olefins was produced.



Having shown that the addition of dinitrogen tetroxide to olefins proceeds by a free-radical mechanism, it was therefore of interest to examine the stereochemistry of the process, especially as this might

throw some light on the question of the stereochemistry of radical addition reactions as a whole. Dinitrogen tetroxide has a particular advantage over hydrogen bromide in this respect, in that both halves of the addendum are easily recognised after addition.

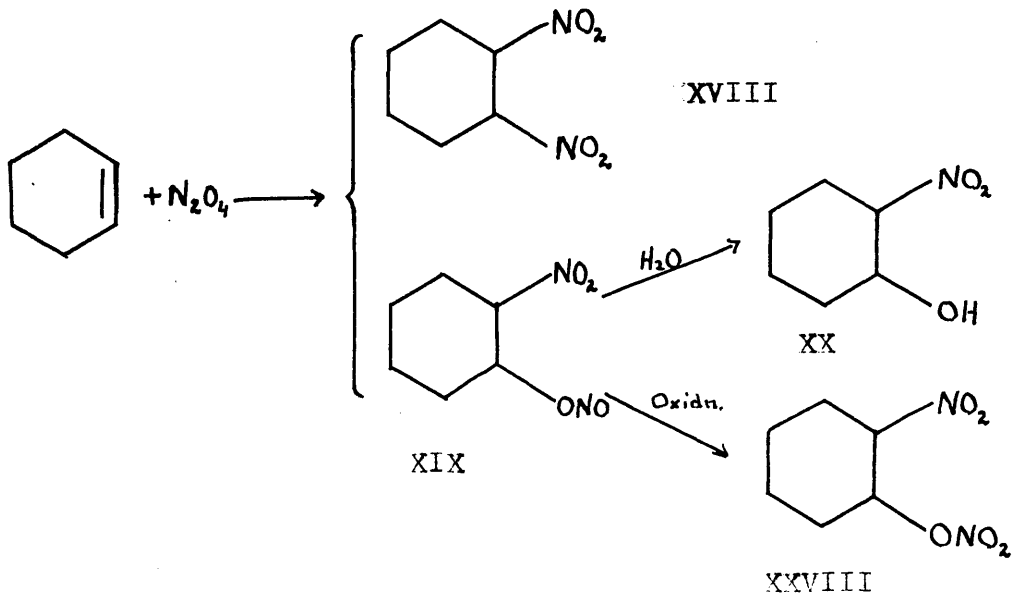
The selection of a cyclic olefin as the unsaturated component is desirable as it precludes the possibility of cis-trans interconversion, due to free-rotation, which is possible in acyclic systems. With this in mind, cyclohexene was first chosen as olefin moiety.

cycloHexene

Another consideration which led to the choice of cyclohexene as the olefin component was the fact that the stereochemistry of the isomeric (d l) cis and trans-2-aminocyclohexanols and their derivatives had been thoroughly elucidated by the work of McCasland and his associates[51], by Johnson and Schubert[41], and by Fodor and Kiss[29]; and it seemed possible that a stereospecific reduction of the nitro-group of the 2-nitrocyclohexanol produced by the reaction to an amino-group could be realised. After a number of unsuccessful attempts, it was found that catalytic

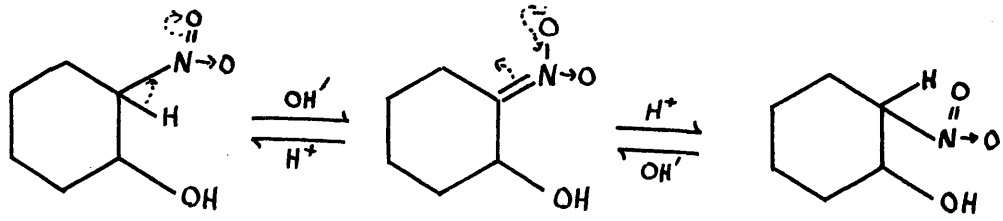
hydrogenation over palladium on charcoal gave the desired stereospecific reduction.

Levy had reported that the 2-nitrocyclohexanol obtained from the reaction of dinitrogen tetroxide with cyclohexene could be induced to crystallise[49e], and it seemed likely that this crystalline alcohol would be isomerically pure. The reaction of dinitrogen tetroxide with cyclohexene was therefore carried out by distilling the tetroxide in a stream of nitrogen into the olefin in ether at 0°. Nitrogen was used as carrier gas to suppress oxidation of 2-nitrocyclohexylnitrite (XIX) to the corresponding nitrate (XXVIII), which Levy had shown to be favoured by oxygen[49a]. After removing the solvent in the falling-film evaporator, the 2-nitrocyclohexanol (XX) was separated by making use of its water-solubility.



Catalytic reduction of a crystalline sample of the alcohol, followed by N-benzoylation[48] gave pure d l - trans-2-benzoylaminocyclohexanol, identical with an authentic specimen prepared by the method of McCasland and his colleagues[51]. Some of the 2-nitrocyclohexanol isolated from the reaction was therefore submitted to the same hydrogenation and benzoylation procedure. Fractional crystallisation of the N-benzoyl derivatives gave a sample of pure d l-cis-2-benzoylaminocyclohexanol, identical with an authentic specimen[51]. The isomeric composition of the mixture of benzoyl derivatives was therefore determined by thermal analysis. This gave the result that the 2-nitrocyclohexanol isolated from the reaction was an isomeric mixture with a cis:trans ratio of 41.8:58.2.

From a comparison of the infra-red spectra, it was noticed that this isomeric ratio, of the alcohol isolated from the reaction, was very close to that of a sample which had been dissolved in alkali and regenerated by the method of Kornblum and Graham with 20% aqueous urea acetate[46], which would have the isomers in the thermodynamic equilibrium mixture.



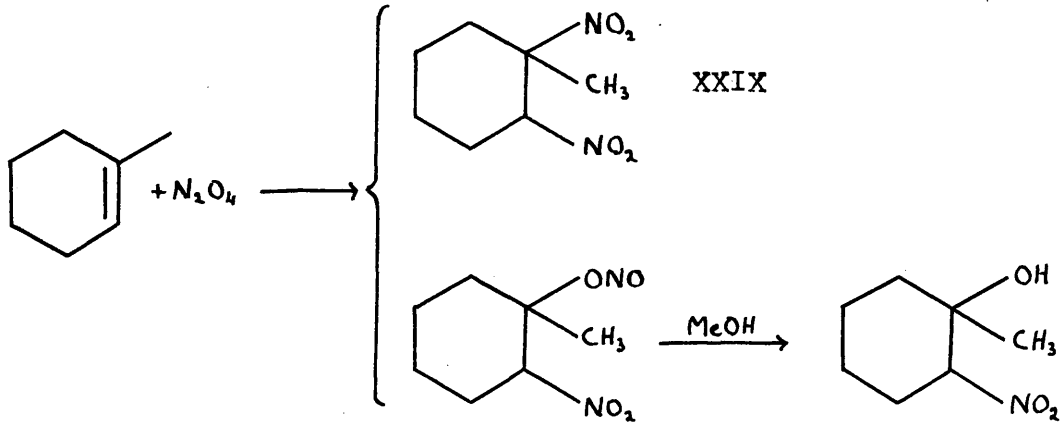
To show that the alcohol isolated had the same stereochemical composition as that formed in the reaction, some of the known trans-2-nitrocyclohexanol was submitted to the working-up process, the conditions being as close a simulation as possible of those pertaining after the reaction. It was recovered unchanged in 90% yield, showing that the result obtained for the isomeric composition is significant.

1-Methylcyclohexene

An analysis of the results of Goering and his collaborators[32,33] in relation to that above showed that the main difference in substrate was in the degree of substitution of the double-bond; for Goering had had, perforce, to use a trisubstituted olefin,

whereas the simplest choice, a disubstituted olefin had been used above. It was therefore decided to examine the reaction of dinitrogen tetroxide with 1-methylcyclohexene.

Under similar conditions to those used for cyclohexene, dinitrogen tetroxide reacted smoothly with 1-methylcyclohexene. The reaction was worked up by stripping off the solvent and solvolysing the 1-methyl-2-nitrocyclohexyl nitrite XXX with methanolic urea solution. This method was employed to obviate the risk of hydrolysis with alkyl-oxygen fission, which might occur with the tertiary ester. Allen has shown that such alkyl-oxygen fission occurs only very rarely, and that methanolysis occurs with retention of optical activity[2].



XXX XXXI

As in the cyclohexene experiment, the 1-methyl-2-nitrocyclohexanol XXXI was separated by using its water solubility. Catalytic hydrogenation to the amine and subsequent benzoylation gave 1-methyl-trans-2-benzoylaminocyclohexanol, identical with a specimen prepared by ammonolysis of 1-methyl-1:2-epoxycyclohexane[53] followed by benzoylation. The trans stereochemistry of the synthetic specimen depends on the well-known rule regarding trans opening of epoxides. The alcohol fraction was carefully checked for any traces of 1-methylcis-2-nitrocyclohexanol, but none could be detected.

When the isolated nitro-alcohol was tested for thermodynamic stability by equilibration with base, it was recovered substantially unchanged (a small amount of a carboxylic acid was formed, possibly by dealdolisation) showing that the trans isomer is the thermodynamically stable one. Deuterium exchange experiments were therefore carried out, and these showed that under acid conditions, as present during the working-up, about 1.3 atoms of deuterium were introduced after 18 hrs. Since one of these atoms, the hydroxylic one, is introduced instantaneously,

the remaining 0.3 atom must have been introduced by enolisation of the nitro-group, which has therefore undergone thermodynamic equilibration to the extent of 30% in 18 hours. However, during the working-up, the nitro-alcohol was only exposed to acid catalysis for 2 to 2½ hrs., and hence should only have suffered equilibration to an extent of 3½ to 4%. This means that the amount of 1-methyl-*cis*-2-nitro-*cyclo*hexanol present can not have exceeded a few percent, and that the reaction of dinitrogen tetroxide with 1-methyl*cyclo*hexene is nearly stereospecifically *trans*.

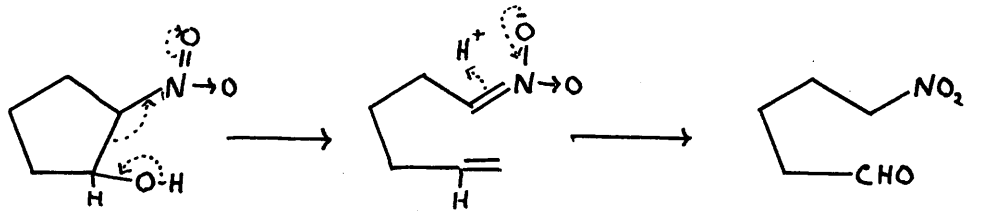
cyclo*Pentene*

Since five-membered rings are nearly planar, whereas six-membered ones are buckled, it was felt that ring size might have an effect on the stereochemistry of radical addition, and so it was decided to examine the reaction of dinitrogen tetroxide with *cyclo*pentene.

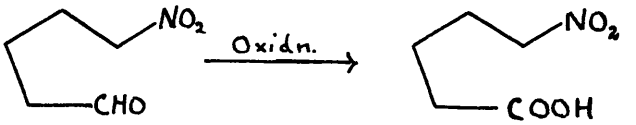
The reaction proceeded smoothly when oxygen was used as carrier with the dinitrogen tetroxide, but gave unstable products when nitrogen was used. The

products were worked-up as for 1-methylcyclohexene. The infra-red spectrum of the crude water soluble fraction showed that appreciable quantities of a carboxylic acid were present. Extraction with aqueous bicarbonate solution followed by distillation gave almost pure 2-nitrocyclopentanol, XXXII. Catalytic hydrogenation followed by p-nitrobenzoylation gave a mixture of the known[52] isomeric cis and trans-2-p-nitrobenzoylaminocyclopentanols. Fractional crystallisation gave a sample of pure trans-2-p-nitrobenzoylaminocyclopentanol, which was converted by the method of McCasland and Smith into the cis isomer[52]. The isomeric composition of the amino-alcohol mixture was determined by thermal analysis, which gave a cis: trans ratio of 16:84.

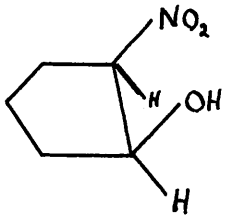
It may be however that the figure arrived at for the amount of cis isomer should be regarded as a minimum, for it seems likely, though there is no definite proof, that the acid, referred to above, arose in the following manner.



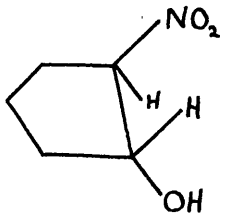
XXXII XXXIII



The reversed aldol step XXXII ⟶ XXXIII almost certainly requires that the four participating centres be co-planar, and this condition is only fulfilled in the cis alcohol, which would thus be preferentially destroyed.



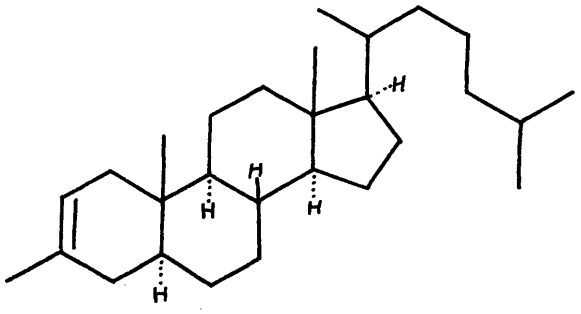
cis



trans

3-Methylcholest-2-ene

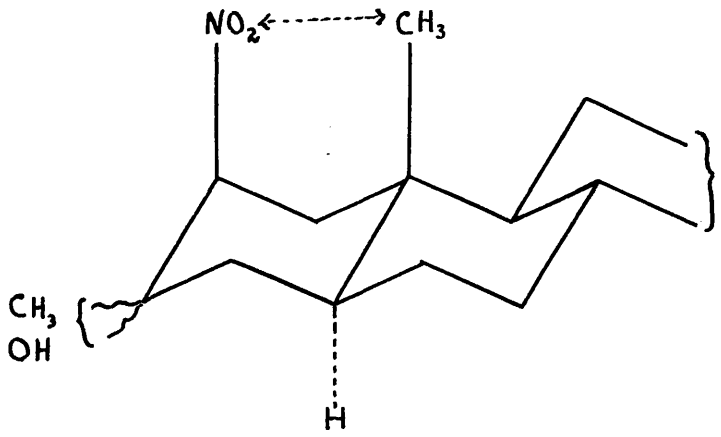
Goering and his associates have postulated that, in cyclohexane systems, the initial attack of a radical on a double-bond occurs axially[33,34], as is the case with heterolytic addition. It is very probable that their postulate is correct, as such an approach allows maximum overlap with the π electrons of the double-bond. In order to obtain some information concerning the conformation of the addition process, the examination of the reaction products with a conformationally rigid olefin was desirable, and it was decided to use the steroidal olefin 3-methylcholest-2-ene, XXXIV.



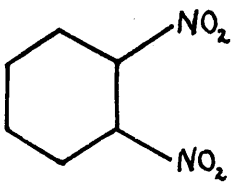
XXXIV

Dinitrogen tetroxide reacted smoothly with the olefin in ether at 0°C. In the presence of oxygen, the products consisted solely of a mixture of 3-methyl-2:3-dinitrocholestane and 3-methyl-2-nitrocholestan-3-yl nitrate, all the initially formed nitrite having been oxidised to nitrate. When the reaction was carried out under nitrogen, only a little oxidation occurred, and the product consisted mainly of a mixture of 3-methyl-2-nitrocholestan-3-yl nitrite and the dinitro compound. As with 1-methylcyclohexene, the nitrite was solvolysed with methanolic urea solution to avoid alkyl-oxygen fission. The nitro-alcohol and dinitro compound were separated by 50 stage counter-current distribution between iso-octane and β-methoxyethanol; after chromatography on silica-gel had been found to dehydrate the alcohol. It had been intended to compare the amino-alcohol produced by reduction of the nitro-alcohol with those prepared by ammonolysis of the olefin epoxides, and so determine the conformation; however it proved impossible to perform this reduction under stereospecific conditions. If, as was postulated, the nitro-group at the 2 position has entered axially, this

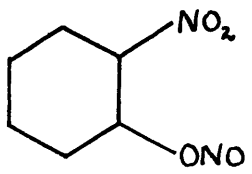
difficulty of reduction may be due to the steric interaction of the nitro-group with the methyl-group at the 10 position; a 1:3-diaxial interaction.



Formula Sheet for Chapter 2.



XVIII



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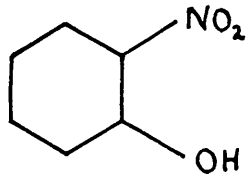

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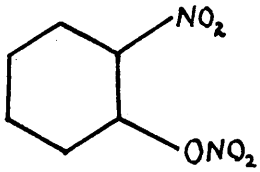
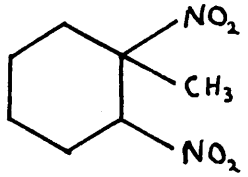


XXVIII



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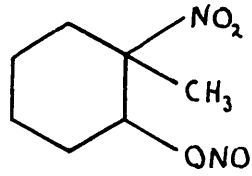
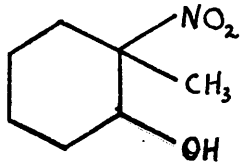


XXX



XXXI

CHAPTER 3

The Reaction of Nitryl Chloride with Olefins

The Reaction of Nitryl Chloride with Olefins

The reaction nitryl chloride with unsaturated organic compounds was first studied by Steinkopf and Kühnel in 1942[74]. Until then very little work had been done with this reagent, because no ready method of preparation was available. Steinkopf and Kühnel found that like nitrosyl chloride, already of wide application for characterising double-bonds, nitryl chloride added directly to the unsaturated linkage of a variety of substituted and unsubstituted olefins and acetylenes to give vicinal chloronitro compounds. The orientation of addition with unsymmetrical olefins was with the nitro-group on the carbon with more hydrogen, except for styrene and phenyl acetylene, where it was on the same carbon as the phenyl group. However their orientation for phenyl acetylene has been criticised by Freeman and Emmons who repeated the reaction and obtained α-chloro-β-nitrostyrene as the only product containing a nitro-group[30]. The addition reaction with nitryl chloride was later extended to a few other olefins by Brintzinger and Pfannsteil[17]; but neither they nor Steinkopf and Kühnel made any comments on either mechanism or stereochemistry.

A mechanism was first proposed for the reaction by Schechter, Conrad, Daulton and Kaplan as a result of their study of the orientation of the addition of nitryl chloride to acrylic systems[62]. Their results are summarised below.

$$NO_2Cl + CH_2{:}CH.R \longrightarrow \begin{cases} O_2N.CH_2.CHCl.R \\ Cl.CH_2.CHCl.R \\ O_2N.CH_2.CH(R).CH_2.CHCl.R \\ O_2N.CH_2.CH.X.R \\ (X = ONO,\ NO_2) \end{cases}$$

$$(R = CO_2H.CO_2Me.CN)$$

Now, whereas in unsymmetrical olefins with electron releasing groups attached to the double-bond, the addition of nitryl chloride by an ionic mechanism, after heterolysis to NO_2^+ and Cl^-, is consistent with the observed orientation[56]:

$$NO_2^+ + CH_2 = CH.CH_3 \longrightarrow O_2N.CH_2 - \overset{+}{C}H.CH_3$$

(or equivalent)

$$O_2N.CH_2 - \overset{+}{C}H.CH_3 + Cl^- \longrightarrow O_2N.CH_2.CHCl.CH_3$$

for acrylic systems, such a mechanism does not explain the observed orientation.

$$NO_2^+ + \overset{\delta+}{CH_2} = \overset{\delta-}{CH} \longrightarrow CO_2Me \longrightarrow \overset{+}{C}H_2 - CH(NO_2).CO_2Me \downarrow \text{Products.}$$

Similarly, an ionisation of nitryl chloride to NO_2^- and Cl^+, shown by Batey and Sisler to be as ready as that to NO_2^+ and Cl^-,[9] not only does not explain the observed orientation with simple olefins; but does not explain why, in additions to acrylic systems, no α-chloro-β-nitrito- or β-hydroxypropionate is formed. Hence, because of the insensitivity of orientation to electromeric effects, and because of the slight telomerisation observed in acrylic systems, Schechter and his fellow workers suggested that "the addition of nitryl chloride to acrylic systems (and possibly vinyl halides and unsymmetrical olefins) involves essentially a homolytic process"[62].

It was therefore of interest to study the reaction in parallel with that of dinitrogen tetroxide, since it was likely that nitrogen dioxide radicals were a common intermediate in each.

cycloHexene was chosen as the olefin moiety in order to avoid complications introduced by cis-trans isomerism of the double-bond in acyclic alkenes. cycloHexene had been shown by Steinkopf and Kühnel to give 2-chloro-1-nitrocyclohexane[74], when reacted with nitryl chloride, and Price and Sears have shown that 1:2-dichlorocyclohexane and nitrosite are also produced in the reaction[56]. It seemed possible that this dichloride was formed from cyclohexene and molecular chlorine produced by the reaction

1. $$Cl. + NO_2Cl \longrightarrow Cl_2 + NO_2$$

which has been shown to be a rapid reaction in the thermal decomposition of nitryl chloride[79]. In order to minimise this possibility, the concentration of nitryl chloride in the reaction mixture was kept as low as possible by distilling it into the solution of cyclohexene in ether. However, as will be shown later, it would appear that the reaction 1. still occurred to a considerable extent. The products isolated and their yields (as molar percentages) are given in Table IV.

TABLE IV

Compound	Yield
2-chloro-1-nitrocyclohexane XXXV	41.2
1:2-dichlorocyclohexane XXXVI	26.4
2-chlorocyclohexyl nitrate XXVI	6.3
2-chlorocyclohexanol XXV	7.7
2-nitrocyclohexanol XX	5.4
1-chloro-2-nitrosocyclohexane dimer	2.8
1-nitro-2-nitrosocyclohexane dimer	7.6
cyclohexen-3-ol XXXVIII	2.7

Total yield based on nitryl chloride = 83%.

As in the dinitrogen tetroxide-bromotrichloromethane experiment, the analysis was carried out mainly by infra-red spectrometric methods. The alcohols were removed from the mixture by using their solubility in water, and the remaining three liquid components were estimated from the infra-red spectrum, which is given in Table V together with those of the pure components. The stereochemistry of the

TABLE V

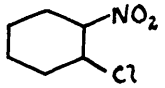
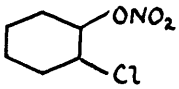
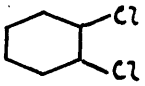
Mixture	 A	 B	 C	Assignment
1637 m.s.		1633† v.s.		B
1557 s.	1557† v.s.			A
1450 m.s.	1450 m.s.	1450 m.s.	1448 m.s.	Common
1374 m.s.	1374 s.			A
1352 m.	1352 m.		1360 v.w.	A
1336(sh.)		1338 w.	1344 w.	B
		1324 m.		
1298(sh.)	1300 m.			A
1280 m.s.		1278 v.s.	1282 w.	B + C
1242 v.w.	1242 w.		1262 v.w.	A
	1220 v.w.	1220 w.		
1215 m.			1210 m.	Common
1204	1206 v.w.	1206 w.	1204	
1132 v.w.			1139 v.w.	C
1118 w.	1118 w.		1122 v.w.	A + C
		1012 m.		
1008 w.	1008,1000 w.		1008 w.	Common
982 w.			981† m.	C
951 w.	950 v.w.	949 m,		A + B
923 w.	923 w.			A
909 w.		914 w.	908 m.	C + B

TABLE V (contd.)

Mixture	A	B	C	Assignment
901 w.	900 m.			A + B
		894(sh.)		
872 m.		874 s.	863 w.	B
858 m.		857 s.		B + C
844 m.		844 s.	843 m.	B + C
819 w.		819 v.w.	819 m.	C + B
811 w.	810 m.	808 w.		A + B
758(sh.)	758(sh.)			A
743 m.s.	747 m.s.	747 m.	742 m.s.	Common
735 m.s.	735 m.s.		736 m.s.	Common
		713 w.		
694 m.	693 m.	696 m.	696 m.s.	Common

Key. v.s. = very strong band
s = strong
m.s. = slightly stronger than medium
m. = medium strength band
w. = weak
v.w. = very weak
(sh.) = shoulder (band not resolved).

Bands marked † were used for quantitative analysis.

dichloride, after isolation by distillation and chromatography on silica-gel, was estimated by infra-red methods. The isomeric compositions of the 2-chlorocyclohexanol XXV and the 2-nitrocyclohexanol XX fractions were also estimated infra-red spectrometrically. The results of these three estimations are given in Table VI.

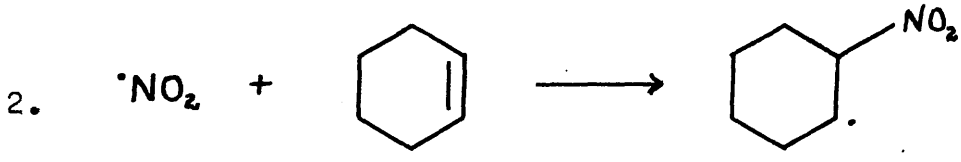
TABLE VI

Compound	band(cm^{-1})	% cis	% trans
2-chlorocyclohexanol	809	38.6	-
	796	-	62.3
2-nitrocyclohexanol	862	-	62.3
1:2-dichlorocyclohexane	885*	no absorbtion detected.	

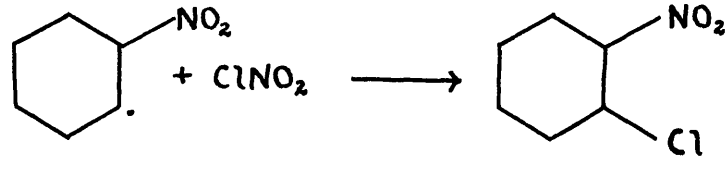
* cis-1:2-dichlorocyclohexane absorbs strongly at 885 cm^{-1}. [76].

The observed products of the reaction, which are most easily explained by a homolytic mechanism, together with the evidence of Schechter and his associates clearly shows that the reaction is a free-

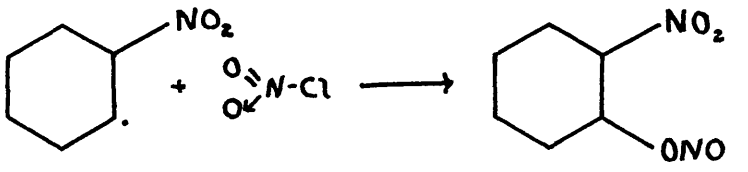
radical one. Now nitryl chloride has rather a high heat of dissociation for the nitrogen-chlorine bond [D (NO_2 - Cl) = 29.5 Kcal][79] and so it seems unlikely that initial homolysis to .NO_2 and .Cl proposed by Schechter[62] occurs. It is much more probable that the reaction, like that of nitric oxide and olefins, is catalysed by nitrogen dioxide, which is formed during the preparation of nitryl chloride and which is not readily removed. Hence the reaction is most probably of the radical-chain type; the initiating step being, as with dinitrogen tetroxide, the addition of nitrogen dioxide to the olefin.

2. 

The chain steps then involve reaction of this radical with nitryl chloride either at chlorine or at oxygen,

3a. 

XXXV

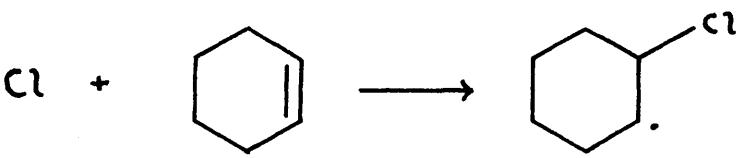
3b. 

XIX

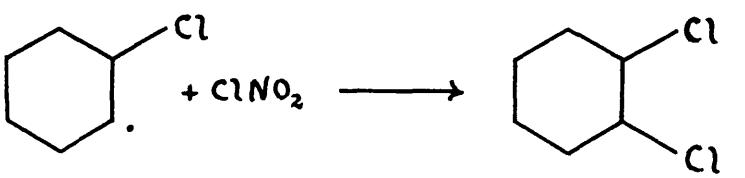
giving either 2-chloro-1-nitrocyclohexane XXXV and a nitrogen dioxide radical to complete the cycle, or 2-nitrocyclohexyl nitrite XIX and a chlorine atom. This chlorine atom may then either undergo reaction 1.,

1. $Cl\cdot + NO_2Cl \longrightarrow Cl_2 + NO_2$

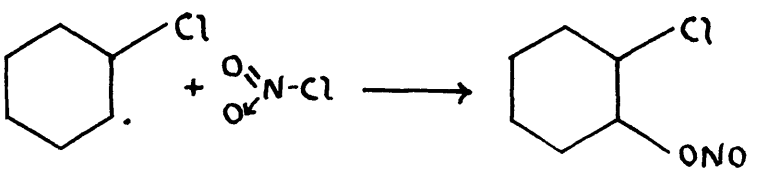
or associate with a cyclohexene molecule to give a chlorocyclohexyl radical,

4. 

which can then react with nitryl chloride in reactions analogous to 3a and 3b.

5a. 

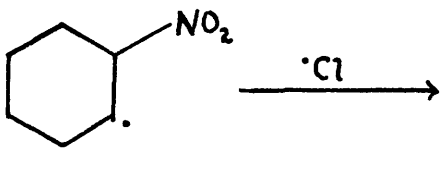
XXXVI

b. 

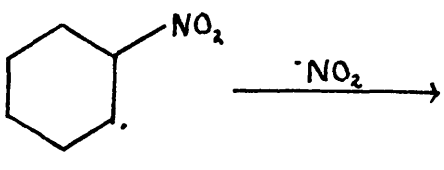
XXIV

That reaction 1. predominates may be inferred from the observed stereochemistry of the 1:2-dichlorocyclohexane XXXVI isolated. If it were formed by the radical reaction 5a one would expect it to have the same stereochemistry as the 2-chlorocyclohexyl nitrite XXIV. As it does not do so, it is more likely that it arose by heterolytic (trans) addition of chlorine, produced by reaction 1., to cyclohexene. From the ratio of dichloride XXXVI to the sum of 2-chlorocyclohexanol XXV and 2-chlorocyclohexyl nitrate XXVI it would appear that reaction 1. is about twice as fast as reaction 4. under the experimental conditions. The ratio of the rate constants is certainly considerably greater than two because the concentration of nitryl chloride is very low compared with that of cyclohexene.

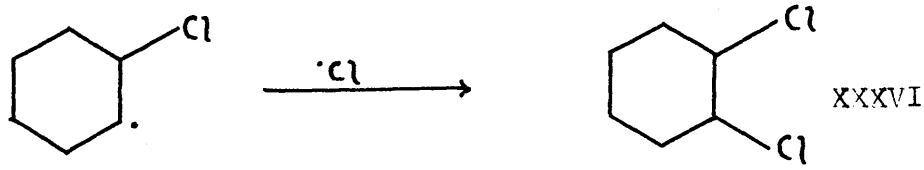
If the second step in the reaction involved radical-radical combination instead of a transfer step,

6a. 

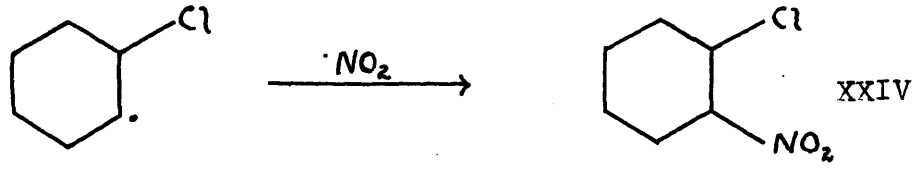
XXXV

b. 

XIX

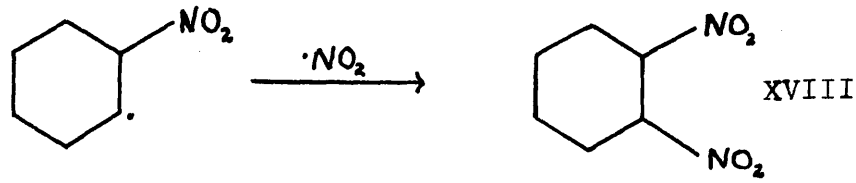
7a. 

XXXVI

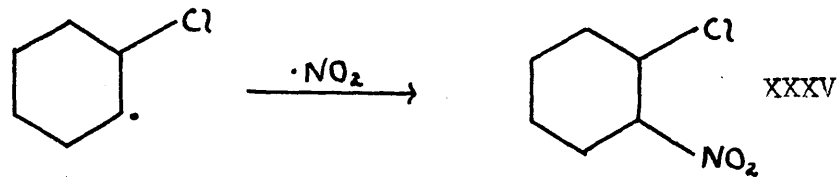
b. 

XXIV

one would expect from reactions 6b and 7b to get the alternate possibilities, as occurs with cyclohexene and N_2O_4[49e]

6b.(ii) 

XVIII

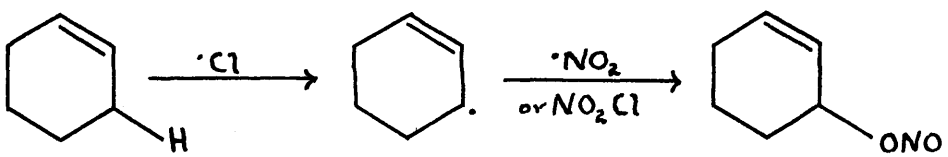
7b.(ii) 

XXXV

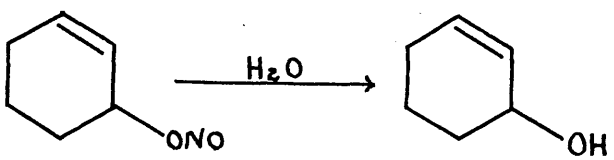
Of these two reactions, 6b(ii) and 7b(ii), only the first gives a product which does not arise by some

other mechanism as well, and hence would be detectable. No trace of 1:2-dinitrocyclohexane XVIII, which if present would absorb at 1134 and 904cm^{-1}, was found, which shows that a radical-radical association step is of little importance. Although it must be admitted that towards the end of the reaction an appreciable concentration of dinitrogen tetroxide, from reaction 1., must be present.

The formation of cyclohexen-3-ol XXXVIII probably occurs by the abstraction of an allylic hydrogen atom from cyclohexene, followed by reaction of the allylic radical with nitryl chloride or nitrogen dioxide to give cyclohexen-3-yl nitrite XXXVII, which hydrolyses during the working-up.

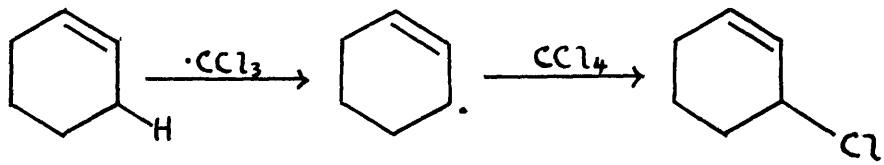


XXXVII



XXXVIII

Since no cyclohexen-3-ol is formed in the reaction of dinitrogen tetroxide with cyclohexene, it is most likely that the hydrogen abstraction is performed by a chlorine atom. A parallel for the reaction may be found in that observed by Kooyman and Farenhorst, in which trichloromethyl radicals abstract allylic hydrogen atoms from cyclohexene, leaving an allylic radical that is sufficiently reactive to remove a chlorine atom from carbon tetrachloride[45].

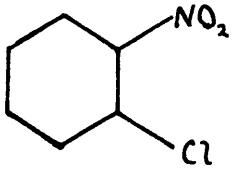


The formation of 'nitrosite' can only be explained by the formation of nitric oxide during the reaction, followed by its addition to an alkyl radical[16]. One source of nitric oxide formation may be the oxidation of nitrite esters to the corresponding nitrates;

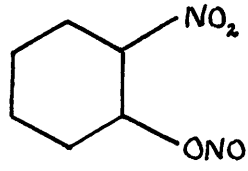
$$R - ONO + NO_2 \longrightarrow \dot{R}ONO_2 + NO$$

but this cannot be the only source for more nitrosite than nitrate ester is produced.

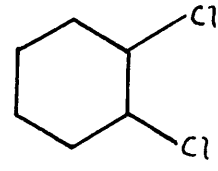
Formula Sheet for Chapter 3.



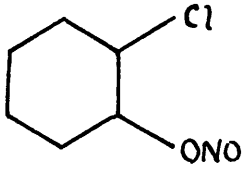
XXXV



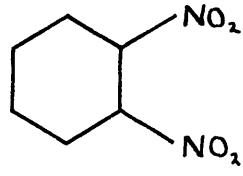
XIX



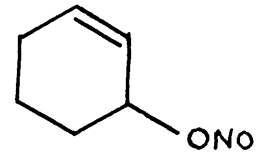
XXXVI



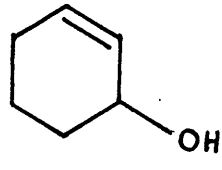
XXIV



XVIII



XXXVII



XXXVIII

CHAPTER 4

The Stereochemistry of Radical Addition

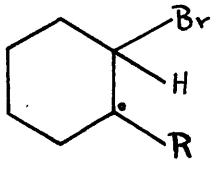
The Stereochemistry of Radical Addition

During the last three years, a number of significant papers have been published on the problem of radical addition to olefins, and they may readily be separated into two groups: those which record stereospecific additions, and those which report non-stereospecific additions.

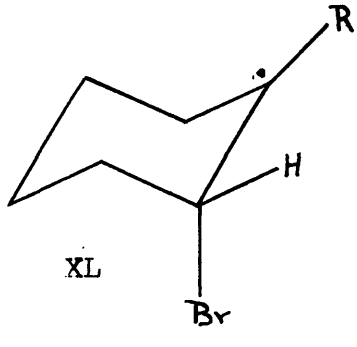
The first group has been the work of Goering and his collaborators and commenced with the publication, mentioned in the introduction, of their work on the addition of hydrogen bromide to 1-substituted cyclohexenes[32]. Their postulate of a 3-membered, configuration holding, ring type of intermediate seems untenable in the light of the evidence of Steinmetz and Noyes on the bromine atom catalysed isomerisation of cis and trans dibromoethylene[75]. They showed that these two olefins are readily interconverted by bromine atoms, with a barrier to isomerisation of not less than 3 kilocalories.

This was apparently realised by Goering, for when (in 1955) he published further evidence supporting the stereospecificity of the addition of hydrogen

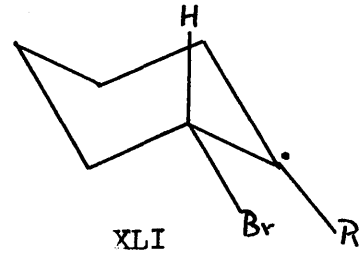
bromide to 1-halocyclohexenes[33], he only briefly mentions ring formation as a possible explanation; and advances the hypothesis that, owing to dipole-dipole interaction, the more stable conformation of the radical XXXIX, formed by the addition of a bromine atom to a 1-substituted cyclohexene, may be that in which the bromine at C2 is axially and the halogen at C1 equatorially oriented XL. This explanation however is not necessarily valid for 1-methylcyclohexene, where there is no dipole interaction.



XXXIX



XL



XLI

XL more stable than XLI.

Goering also advances the hypothesis that the radical XL is the one that is first formed by the addition of a bromine atom, and that it reacts more rapidly than it inverts to XLI, which amounts to

kinetic control of the products. It can readily be seen that Goering had thus proposed the only three possible explanations for the stereochemistry of radical addition i.e. a non-classical radical, thermodynamic control and kinetic control.

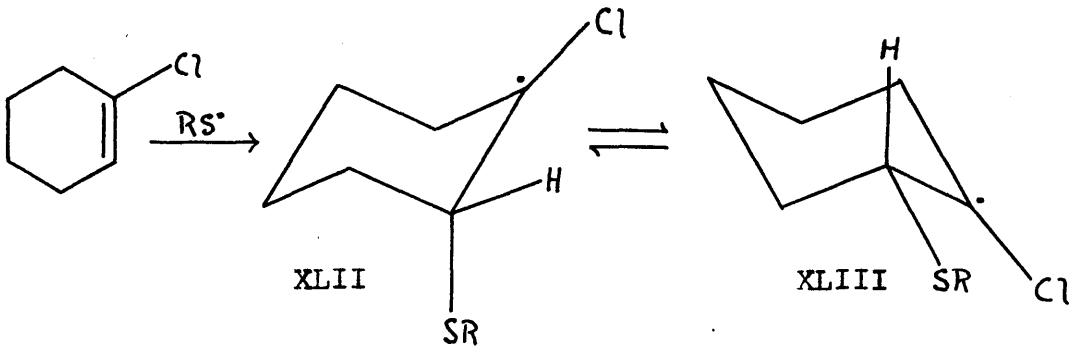
About the same time as this, Khan reported that nitrogen dioxide was an active agent for the isomerisation of aliphatic double-bonds[42], and postulated the reversible formation of an olefin-radical π complex which permitted free rotation. Thus a situation arose where these two workers each postulated an olefin-radical π complex, one giving the complex the property of free-rotation, and the other that of configuration retentivity. It would therefore seem that such a non-classical radical has no existence, and that Khan's results are due to the reversibility of the initial radical addition step. This is in accord with the results of Sivertz, Andrews, Elsdon and Graham, who found that the radical addition step in the reaction of hydrogen bromide and of thiols with olefins was reversible and <u>not</u> rate determining[66].

$$RS\cdot + \rangle C = C\langle \rightleftharpoons RS - \underset{\wedge}{C} - \dot{C}\langle$$

Although recent evidence presented by Hammond, Boozer and their associates would indicate the possibility of the formation of a loose π complex between radicals and aromatic systems[37], the results of Goering and his colleagues on the addition of thioacids to 1-chlorocyclohexene[34] finally exclude the possibility of a three-membered ring intermediate; for one would expect that a sulphur atom, having more electrons and orbitals available, would form such an intermediate more readily than bromine, whereas the observed stereospecificity is considerably less than that for hydrogen bromide. Goering and his associates found that in additions of thiophenol, hydrogen sulphide and thiolacetic acid to 1-chlorocyclohexene the amount of cis addition (trans product) observed was 5, 14 and 34% respectively; results in accord with those of Bordwell and Hewitt[84] on the addition of thiolacetic acid to 1-methylcyclohexene and 1-methylcyclopentene, in which respectively 15 and 25% of cis addition took place.

Goering explains these results by elaborating his previous postulate of kinetic control. He argues that the radical first formed will have the entering

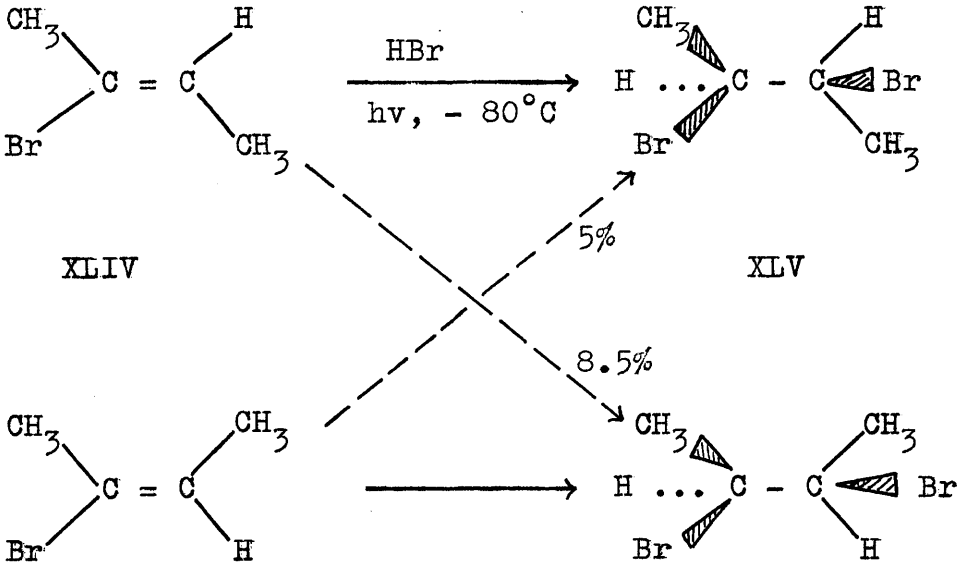
group axial XLII and that this reacts more rapidly than it isomerises to the equatorial form XLIII.



For the form XLII there is a steric advantage to approach of RSH, in the transfer step, to give trans-addition, whereas XLIII gives cis and trans addition products equally readily. Since he observed some cis addition, Goering says that the important factor is radical lifetime, because increased time before reaction leads to greater ring inversion to form XLIII, and points out that when the ratio of addendum to substrate is increased, the percentage of trans addition increases. However, he does not entirely abandon the idea that the radical XLII may be more stable than XLIII.

In a recent note, Goering and Larsen have reported that in hydrogen bromide solution the addition of hydrogen bromide to trans-2-bromobutene-2 XLIV gives

almost exclusively dl-2:3-dibromobutane XLV, the product of trans addition, and cis-2-bromobutene-2 XLVI gives, similarly, meso-2:3-dibromobutane. [35].



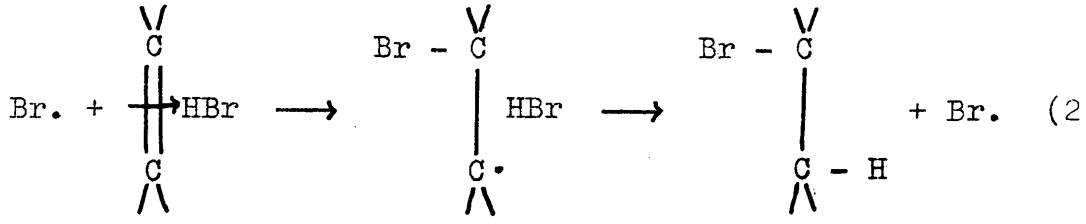
XLIV XLV

XLVI XLVII

While, at first sight, this is definitive evidence in favour of kinetic control, yet it can readily be seen that the experimental conditions were the most favourable possible for ensuring that the transfer step (1) was

$$>C.Br - \dot{C}< + HBr \longrightarrow >C.Br - CH< + Br. \qquad (1)$$

extremely rapid, possibly due to olefin-acid π complexing



(2)

The result would not therefore apply to the general case; indeed Goering has shown that in the addition of hydrogen bromide to 1-bromocyclohexene there is essentially no olefin-acid complex[33].

Of the evidence in regard to free-radical addition reactions which are non-stereospecific, the findings of Campbell and his colleagues and of Freeman and Emmons on the addition of dinitrogen tetroxide to acetylenes has already been mentioned[20,30]. The remainder of the evidence has been the work of Skell and his associates. Skell and Woodworth have examined the light catalysed addition of bromotrichloromethane to cis and trans butene-2[67] and found that, under conditions where cis-trans isomerisation did not take place, the same diastereomeric mixture of 1:1 adduct was obtained from each olefin, indicating that the intermediate radical $CH_3.CH(CCl_3).\dot{C}H.CH_3$ had sufficient time to reach equilibrium among its

possible configurations. In an extension of this work, Skell, Woodworth and McNamara have found that the addition of benzenesulphonyl iodide to cis and trans butene-2 also gives a mixture of isomers[71], and that in the copolymerisation of cis and trans-butene-2 with sulphur dioxide, a radical process, the same polymer is obtained from each olefin[72]. Skell[72] states that, for radicals higher than methyl, he would expect the conformation to be that of a low pyramid, due to non-bonded interactions, and concludes that the rate of racemisation of such a radical, by ammonia like inversion, is considerably greater than the rate of reaction of either his growing chain radical with sulphur dioxide or of $CH_3.CH(BsO).\dot{C}H.CH_3$ with benzene sulphonyl iodide.

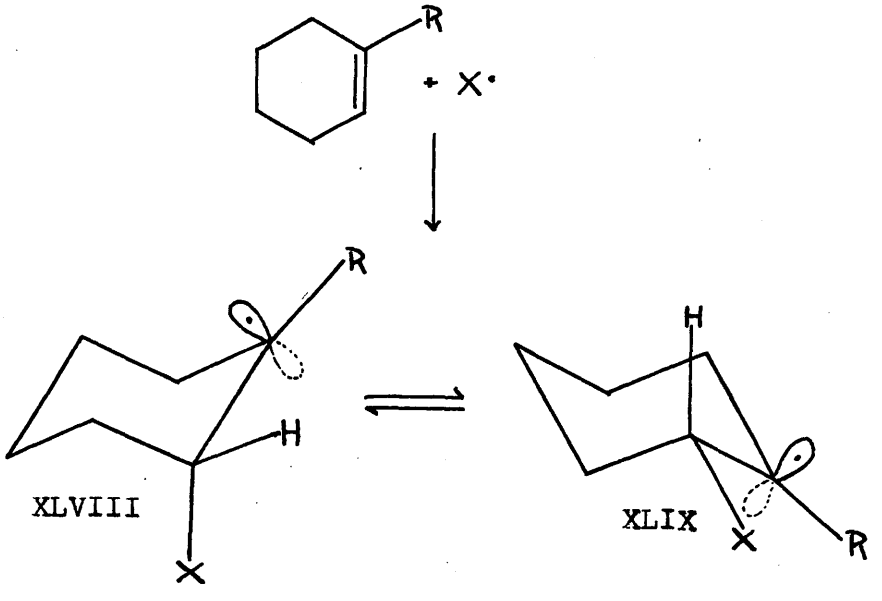
An examination of the results of all the above work together with that on the addition of dinitrogen tetroxide and nitryl chloride to olefins (summarised in Table VII) reveals one striking fact; namely that whereas with trisubstituted olefins nearly stereospecific trans addition is observed, with disubstituted olefins a mixture of cis and trans isomers is obtained. Of the explanations so far advanced, none takes cognisance of this fact, and none alone satisfactorily explains why the substitution of methyl for hydrogen should so profoundly affect the stereochemistry.

TABLE VII

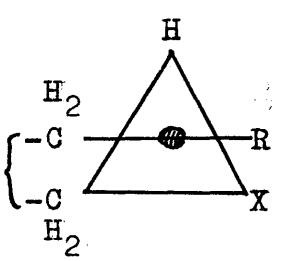
Olefin	Adduct	Initiator	% of trans addition	References
1-Methyl-cyclohexene	HBr	Br	ca. 100	32
1-Bromo-cyclohexene	HBr	Br	99.5	32,33
1-Chloro cyclohexene	HBr	Br	99.7	33
"	PhSH	PhS	94-99	34
"	H_2S	HS	86-92.5	34
"	$CH_3.CO.SH$	$CH_3Co.S$	66-73	34
cycloHexene	N_2O_4	NO_2	58	This work
"	NO_2Cl	Cl	62	"
"	NO_2Cl	NO_2	62	"
1-Methyl-cyclohexene	N_2O_4	NO_2	98	"
cycloPentene	N_2O_4	NO_2	84	"

As it was pointed out in the introduction, the spatial conformation of the free-radical centre must play an important part in the determination of the resultant stereochemistry, and since there is still some uncertainty regarding this, the implications of both a planar and a pyramidal radical will be discussed.

If one considers the addition of a species XY to a cyclohexene derivative, and assumes that the radical produced by addition of X is planar, and that X has approached the double-bond from the direction which allows of maximum overlap on the π electron cloud, i.e. axially, the radical first produced will be XLVIII,



which can either react with XY (or Y) to give product, or can undergo a ring inversion to XLIX. In the form XLVIII there is a marked steric advantage for the consummating molecule (or radical) to approach from the side remote from the group X, leading to <u>trans</u> addition of XY; whereas for form XLIX there is no favoured side for approach, but if attack is from above (in the figure), the group R must pass through a position in which it is totally eclipsed by X in the transition state, and hence attack from below is more likely to succeed, leading to a slightly favoured <u>cis</u> addition. [The figure L gives a diagrammatic view of form XLIX viewed along the $C_1 - C_2$ bond].



L

Hence if ring-inversion were a rapid process one would expect considerable amounts of <u>cis</u> addition. Now for R= Methyl one must assume that ring-inversion is slow compared with reaction, whereas for R= Hydrogen

it must be a competitive step in order to explain the observed results. Since one would expect no difference in the rates of reaction to give product between R = Me and R = H, one must postulate a difference in the rates of inversion XLVIII $\rightleftharpoons$ XLIX between R = Me and R = H. This difference in rate might be attributed to the interaction of the group X with the group R in form XLIX when R = Me. Table VIII gives the distances between X and R, as measured on scale models, for form XLIX.

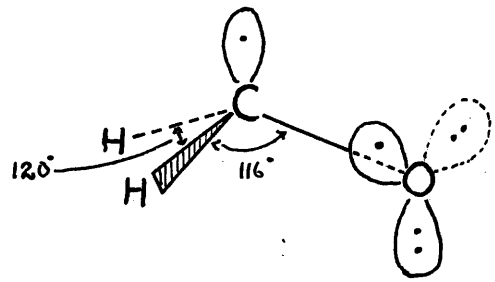
TABLE VIII

Groups	distance observed (Å)	Σvan der Waals radii (Å)	$\Sigma x \frac{100}{130}$ (Å)
Br·····CH_3	3.25	3.95	3.04
Br·····Cl	3.05	3.75	2.9
O_2N·····CH_3	3.0	3.5	2.7
ONO·····CH_3	2.5 min. 3.45 max.	3.4	2.6

The figure Σx 100/130 represents the distance to which the van der Waals envelopes can interpenetrate before interference becomes severe. It can be seen that a

certain amount of interference is observed, which will undoubtedly affect the rate of inversion XLVIII $\rightleftharpoons$ XLIX ; but it seems unlikely that this is sufficiently great to account for the observed difference in stereospecificity of ca. 60% <u>trans</u> for R = H and ca. 100% <u>trans</u> for R = Me,Cl. Hence this explanation involving a planar radical can be seen to suffer from a severe disadvantage.

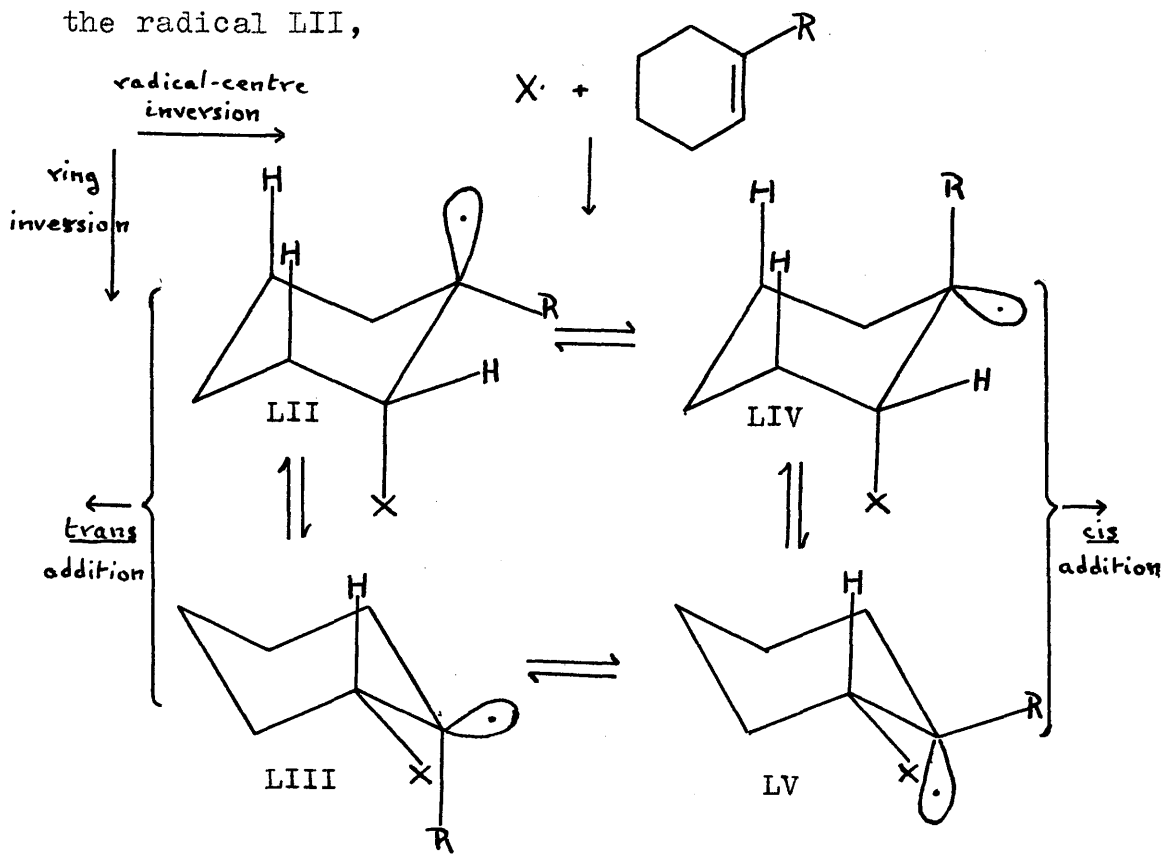
A consideration of the stereochemistry of a radical leads one to the conclusion that an odd-electron is probably equally stable in an sp^2 or in an sp^3 orbital, and hence will take up that form in which the non-bonded interactions are minimised; for although a methyl radical is planar or nearly so[38], the biradical excited state of formaldehyde LI is that of a low pyramid with a staggered ethane-like structure[12a].



LI

Hence one would expect any form such as XLIX, in which there is a non-bonded interaction between R and X, to bend so as to relieve the strain. Any such bending towards a pyramidal radical would thus diminish a difference in stability between R = H and R = Me in form XLIX, and hence also diminish any difference in the rates of inversion.

One must therefore consider the possibility that the radical XLVIII, produced by addition of X to the cyclohexene derivative, is pyramidal. In this case it seems likely that, at the same time as the group X attacks the double-bond axially, the odd-electron is 'squeezed out' in the opposite axial position giving the radical LII,

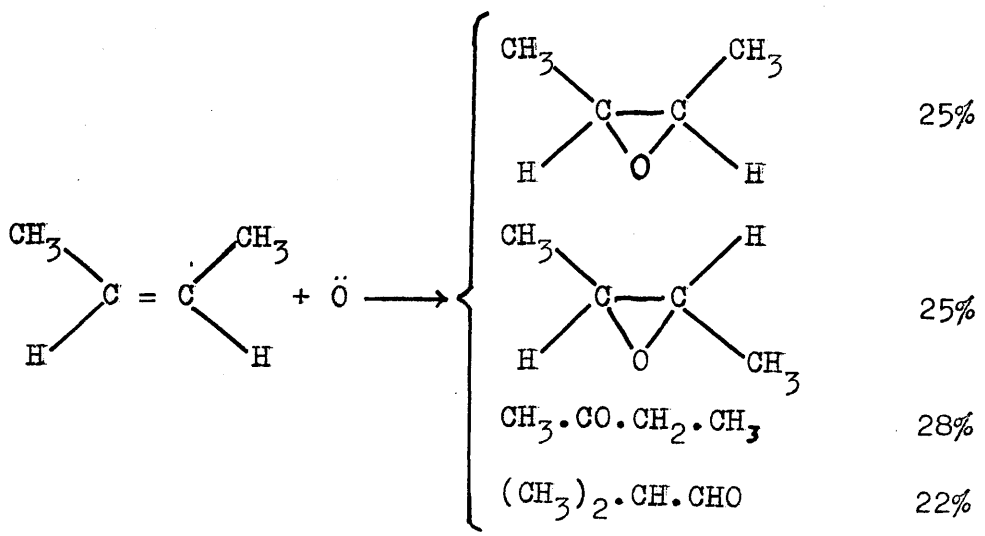


which can either undergo ring inversion to LIII or radical-centre inversion to LIV. One can now postulate that ring-inversion is of comparable speed for both R = Me and R = H, and that it is slow compared to reaction with XY (or ·Y). One can also postulate that the rate of racemisation at the radical centre (i.e. LII $\rightleftharpoons$ LIV or LIII $\rightleftharpoons$ LV) is of comparable dimensions for R = H and R = Me and that it is fast compared with any other step. The difference in stereochemistry will then depend on the relative proportions of the two forms LII and LIV. Now, for R = H, there will be little difference in the stability of the two forms, since neither hydrogen (LIV) nor the odd-electron (LII) will meet any 1:3-diaxial non-bonded interaction. However, for R = Me, Cl, there will be a considerable difference in the stability of the two forms, because in LIV the large group R will meet an appreciable 1:3-diaxial interaction which will diminish the stability of this form. It seems likely that this will be sufficient to drive the equilibrium over in favour of form LII to such an extent that <u>trans</u> addition occurs almost exclusively.

In fact it may be that the radical LIV, in diminishing its non-bonded interactions, becomes planar, the equilibrium for radical-inversion thus lying between the forms LII and XLVIII, and not between LII and LIV, when R = Me. Hence for cyclic systems at least this explanation agrees with the observed facts.

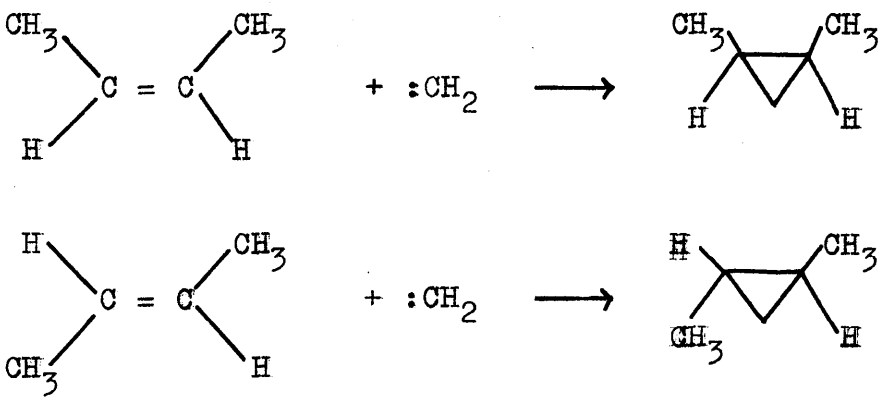
For the addition of thiocompounds one must postulate that the step involving reaction with RSH is slower than for hydrogen bromide or dinitrogen tetroxide, and hence the ring-inversion is able to compete with the transfer step, resulting in more <u>cis</u>-addition.

That some radical reactions are comparatively slow can be inferred from the results of Cvetanović on the addition of excited (biradical) oxygen atoms to <u>cis</u> butene-2[24]. His results are summarised below,



and indicate that the intermediate bi-radical $CH_3.CH.CH.CH_3$ had sufficient time to rotate or undergo migration steps before reacting intramolecularly.

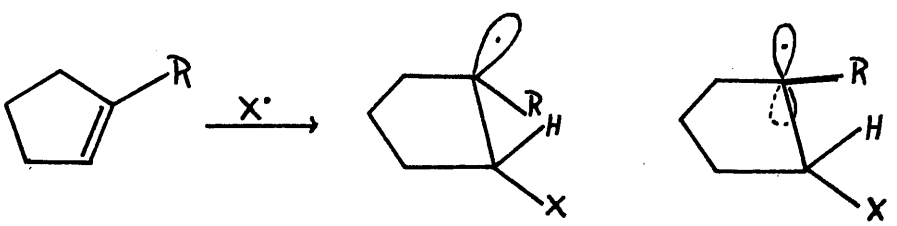
The reaction of methylene and substituted methylenes with olefins[25,26,27,68,69,70,73] may also be a radical process, involving the addition of a bi-radical to a double-bond. However in contrast to the reaction above, the addition of methylene is a stereospecific reaction[68,69,70] giving exclusively cis-addition[27].



The reaction is a very rapid one, and it may either be concerted, the reagent adding simultaneously to both ends of the double-bond, or stepwise, giving an intermediate bi-radical, followed by rapid ring-closure. However it seems unlikely that any experiment sufficiently delicate to distinguish between these

two alternatives will be devised within the foreseeable future.

For cyclopentene systems the above explanation for cyclohexene derivatives also applies. For if the radical LVI, produced by addition of X• to a cyclopentene derivative, minimises its non-bonded interactions, it will assume a planar form LVII at the radical centre.

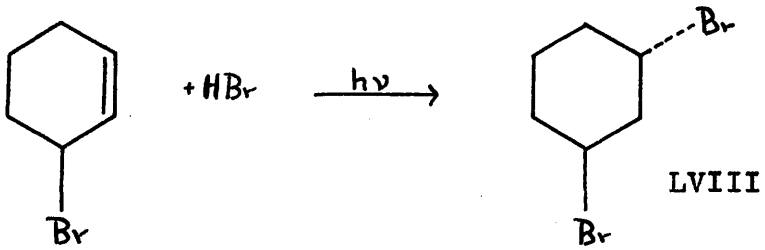


LVI LVII

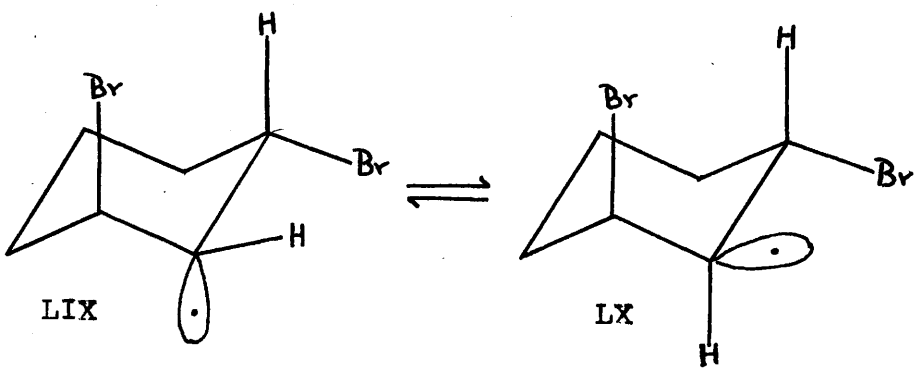
This is because in cyclopentane, being nearly planar, the carbon-hydrogen bonds are eclipsed round the molecule, and a planar radical will relieve two such bond eclipses. Scale models show that a planar radical of this type has a slight steric preference for attack from the side remote from the initially installed group X, and this is sufficient to account for the preponderance of trans addition observed.

While not strictly relevant, a further interesting example of a stereospecific radical addition reaction

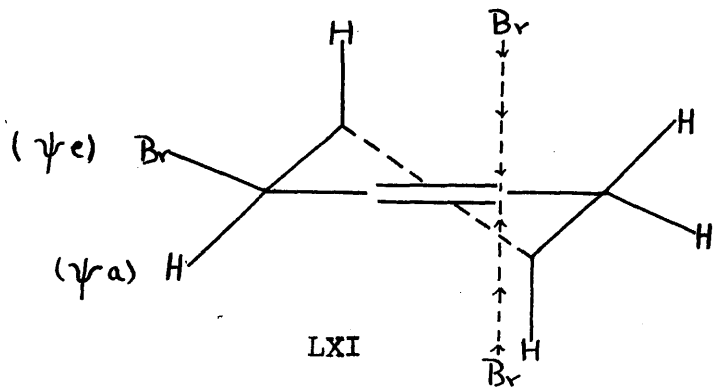
has recently been reported by Kharasch and his co-workers[44]. The addition of hydrogen bromide to 3-bromocyclohexene yields exclusively trans-1:3-dibromocyclohexane LVIII,



It can readily be seen that after the addition of the initial bromine, it matters little whether the consummating hydrogen adds in a cis or a trans relation to it, for the stereochemistry has already been determined LIX, LX.



Hence to explain the stereospecificity of the reaction, one must seek a reason for an initial trans addition of bromine. Scale models show that if the bromine at the 3-position is occupying the more stable pseudo-equatorial position in the initial cyclohexene derivative(LXI), there is a steric advantage for the bromine atom to attack trans to it; and any electrostatic effect that may be operating will tend to enhance the bias towards trans addition.



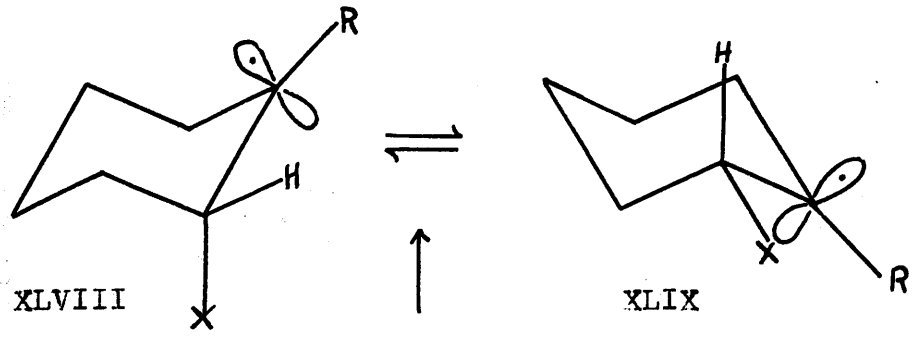
LXI

Should, on the other hand, the bromine at C_3 be occupying the pseudo-axial position, then there is an extremely strong steric advantage in favour of addition trans to it.

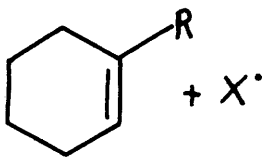
In conclusion it must be admitted that, while the hypothesis advanced above for the stereochemistry of

radical addition reactions explains, for cyclic systems, the observed results, it is not wholly satisfactory, and suffers from the disadvantage that it is not applicable to acyclic systems. It is obvious that more investigation is required, in particular, to try to determine the rate of ring-inversion in cyclohexane derivatives and the rate of racemisation of free-radical centres; but it is difficult, at this stage, to see any method whereby such information can be obtained.

Formula Sheet for Chapter 4.

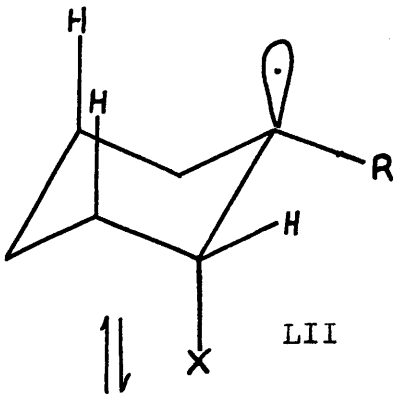


XLVIII XLIX

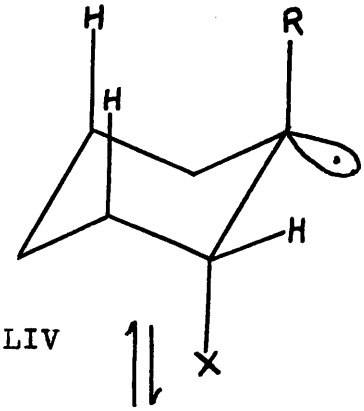


radical-centre inversion

ring inversion



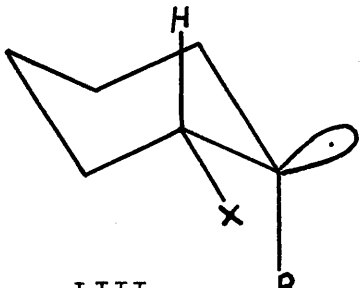
LII



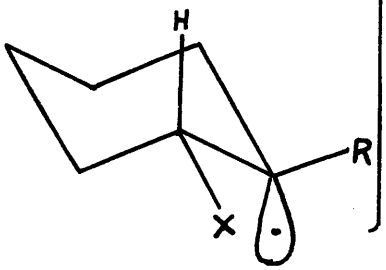
LIV

trans addition

cis addition



LIII



LV

CHAPTER 5

Experimental

Experimental

Reagents

Dinitrogen Tetroxide

It is essential that this be pure[49]. It was prepared, as it was required, by the thermal decomposition of lead nitrate.

$$Pb(NO_3)_2 \longrightarrow PbO + N_2O_4 + \tfrac{1}{2}O_2$$

ANALAR lead nitrate was ground up finely, dried in air at 150 to 160°, mixed with ca. 5 times its bulk of clean, dry silver sand (to aid smooth decomposition) and heated in a furnace to ca. 500°C. The dinitrogen tetroxide evolved was carried out of the furnace vessel in a stream of dry oxygen, passed over phosphorus pentoxide and collected at -80°. The dinitrogen tetroxide was purified by repeated distillation over phosphorus pentoxide in a current of oxygen, until, on condensation at -80°, it was obtained as a colourless crystalline solid. Traces of dinitrogen trioxide give rise to a marked blue colour.

Nitryl Chloride

This was prepared by the reaction of chlorosulphonic acid with anhydrous nitric acid[64].

$$HSO_3.Cl + HNO_3 \longrightarrow NO_2Cl + H_2SO_4$$

30% Oleum (32.3 g.) was added dropwise, with cooling and stirring to fuming nitric acid (20 g.). Chlorosulphonic acid (18.5 ml.) was then added dropwise with cooling and stirring. The nitryl chloride was evolved as a colourless gas and collected in a trap at -80°. It was purified by distillation over phosphorus pentoxide in a stream of dry oxygen. The infra-red absorbtion spectrum (in CCl_4) showed that nitrosyl chloride was absent[18,61]. The ultraviolet absorbtion spectrum was consistent with the presence of 1-2% of chlorine[3] and nitrogen dioxide. The pale yellow colour of the liquid would seem to confirm this.

Ether

Initially anaesthetic ether was used. This was dried over calcium chloride and sodium wire, distilled from phosphorus pentoxide, and stored over fresh sodium wire. Latterly commercial anhydrous ether (M and B) was dried over sodium wire and used without further purification.

cycloHexene

Commercial cyclohexene was distilled, the fraction boiling 80-84° being further purified. This fraction

was refluxed over cupric stearate[31], to decompose peroxides, until there was no further reaction, and then distilled in a nitrogen atmosphere. Fractionation from sodium, in nitrogen, gave cyclohexene b. 82.4-82.5°, which was treated once more with cupric stearate and distilled in nitrogen.

1-Methylcyclohexene

This was prepared by the method of Bartlett and Rosenwald[4].

Redistilled cyclohexanone (200 g., 2 moles) in ether was added to methyl magnesium iodide, prepared from methyl iodide (284 g. 2 moles) and magnesium (48 g., 2 moles), in ether. The resulting crude alcohol was distilled, some dehydration taking place. The mixture of alcohol and olefin was then fractionated, a little iodine having been added to catalyse dehydration. The fraction b. 100-112° was collected and the water separated. The crude 1-methylcyclohexene was extracted with bisulphite to remove ketone (shown to be present by infra-red spectrometry), washed with water and dried. It was then refluxed with cupric stearate (to destroy peroxides) and fractionated from

sodium, in nitrogen, to give 1-methylcyclohexene (70 g., 0.73 mole) b. 107.4-108°/750 m.m. $n_D^{15.5}$ 1.4542. Goering gives b. 108.4-108.7°. n_D^{25} 1.4478[32].

cycloPentene

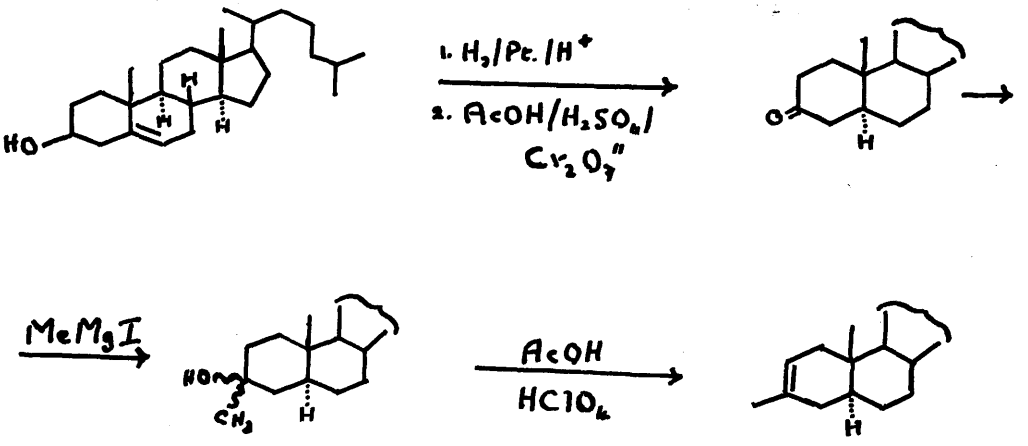
This was prepared by reduction of cyclopentanone followed by dehydration. cf. McCasland and Smith[52].

Redistilled cyclopentanone (1.525 mole) b. 130-2° was hydrogenated over Adams' platinum oxide catalyst (1 g.) at 130-170° and 120 atmospheres. Distillation afforded fore-run (20 g.) b. 125-137°, followed by cyclopentanol (1.259 mole) b. 137-140°, shown by infra-red spectrometry to contain no ketone. The cyclo-pentanol was dehydrated by refluxing with, followed by distillation from, p-toluene-sulphonic acid, to give a mixture of cyclopentene and water. The olefin was separated, dried and refluxed twice over, and distilled from, fresh sodium. Distillation afforded cyclopentene (1 mole) b. 43-44° $n_D^{15.5}$ 1.4258. McCasland and Smith record b. 43-46, n_D^{18} 1.4218[52].

3-Methylcholest-2-ene

This was prepared from cholesterol by the following

series of steps, according to the method of Barton; Campos-Neves and Cookson[7].



Cholesterol (20 g.) in ethyl acetate (700 ml.) was hydrogenated over Adams' platinum oxide catalyst (0.6 g.) at atmospheric pressure: about 10 drops of perchloric acid (ANALAR 70%) was added to catalyse the reaction. The uptake of hydrogen was theoretical after 6-7 hours. The solvent was removed in vacuum, and the product hydrolysed with 5% ethanolic potassium hydroxide for ½ to 1 hour. Cholestanol (17.6 g.) m. 140-2° crystallised out on cooling.

The oxidation stage was carried out exactly as described in 'Organic Syntheses'[17], Cholestanol

(50 g.) gave cholestanone (37.5 g.).

Cholestanone (35 g.) in ether (250 ml.) was added to methyl magnesium iodide (prepared from methyl iodide (14.2 g.) and magnesium (2.4 g.) in ether with stirring. The mixture was refluxed for ½ hr., the Grignard complex decomposed with water and then dilute acid. The ether layer was separated, washed with aqueous bicarbonate and then with water. Evaporation under reduced pressure gave a mixture of the isomeric 3-methyl cholestan-3α and 3β-ols. This crude mixture was dissolved in a slight excess of glacial acetic acid (100 ml.), 12 drops of perchloric acid (ANALAR 70%) added, and heated for 1 hr. at 100°. The resultant mixture was concentrated to small bulk under reduced pressure, and water and then ether added. The ethereal extract was washed twice with aqueous sodium bicarbonate, then with water and evaporated to dryness. The resultant oil was dissolved in petroleum ether (b. 40-60°) and chromatographed on activated alumina. The 3-methylcholest-2-ene (25.9 g.) crystallised on evaporation of the eluent petroleum ether (b. 40-60°) and had m. 81-2°, $[\alpha]_D$ + 72° ($CHCl_3$). Barton et al. give m. 82-3° $[\alpha]_D$ + 74°.[7].

Bromotrichloromethane

Commercial bromotrichloromethane was redistilled, the colourless middle cut, b. 103.9-104.1°, being used.

Reactions

Reactions were carried out at -5 to 0°C in a three-necked round-bottomed flask fitted with a mercury sealed stirrer. The dinitrogen tetroxide was distilled in through a gas inlet tube, fitted with a sintered glass disk, and reaching to the bottom of the flask. The outlet tube was fitted with a guard-tube of fine mesh chloride to prevent inward diffusion of moisture.

Reactions were worked up by removing the solvent under reduced pressure (30-50 m.m. mercury) in a falling film evaporator[49a], and allowing the high-boiling product to fall into either water or methyl alcohol. This minimises the risk of decomposition of the nitro-nitrites[49a].

Identifications and Analyses by Infra-red Spectrometry

Where compounds were identified by infra-red

spectrometric methods, the identification depended on satisfactorily accounting for all the bands in the reference spectrum. The choice of a band for use for quantitative analysis depended on the band chosen being free from interference by any bands belonging to either the same compound or any other component of the mixture. As far as possible strong or fairly strong bands were chosen for this purpose. They were calibrated under standard conditions against solutions of the reference compounds. Where isomeric compositions were determined by infra-red methods, bands were chosen which were characteristic for only one isomer; but where the total isomeric quantity was required, a band common to both isomers, and of as nearly as possible the same intensity for each, was selected.

For bands in the 1500 to 1650cm^{-1} region, solutions were made up in tetrachloroethylene; and for bands below 1100 cm^{-1} solutions were made up in carbon disulphide.

The principal infra-red absorbtion bands of the various reference and other pure compounds are given in the appendix.

Dinitrogen tetroxide with cyclohexene and bromotrichloromethane

Dinitrogen tetroxide (99 millimoles) was distilled, in a stream of oxygen, into a solution of cyclohexene (294 m. mole) and bromotrichloromethane (980 m. mole) in ether (150 ml.) at 0°C. When the addition of N_2O_4 was complete, the green reaction mixture was stirred for ½ hr. and then the volatile components stripped off (in the film-evaporator) and condensed in traps at -80°, the involatile fraction being allowed to fall into water (200 ml.).

Volatile fraction

This was washed with water, dried ($MgSO_4$) and distilled to give a volatile fraction b. 30-104°, and an involatile residue (10.1 g.). The fraction boiling at atmospheric pressure was carefully fractionated to give

1. b. 35° (ca. 100 ml.) ether
2. b. 75-85° (small) contained a little cyclohexene
3. b. 100-104° (91.0 g., 50.5 ml.).

Infra-red spectrometry showed that fraction 3 consisted of a 1% (V:V) solution of trichloronitromethane (total, 3.04 m. mole) in bromotrichloromethane. However,

trichloronitromethane is known to decompose when distilled at atmospheric pressure; hence this value is a minimum.

The involatile residue was shown by infra-red to be a mixture of 1-bromo-2-chlorocyclohexane and 2-chlorocyclohexanol, and so it was combined with the corresponding fraction below.

Involatile fraction.

This was washed several times with aqueous urea solution (to destroy nitrous acid). The aqueous washings (600 ml.) were neutralised to pH5 to 6 with bicarbonate and extracted continuously with ether for 80 hrs. Removal of ether, followed by distillation gave

1. b. 79-80°/18 m.m. (1.9 g.) shown by infra-red to be 2-chlorocyclohexanol (14.1 m. mole).
2. b. 74-6°/0.6 m.m. (0.3 g.), which on careful fractionation yielded a small quantity of cyclohexane-trans-1:2-diol, m. and mixed m. 99°, with infra-red spectrum identical with that of an authentic specimen. The remainder was not identified.

After removal of solvent from the insoluble fraction, a white solid precipitated and was filtered

off (0.25 g.) m. 153-153.5°d., identified as cyclohexene nitrosite (Found C, 45.71; H, 5.87. Calc. for $C_6H_{10}O_3N_2$, C, 45.56; H, 6.37%) Levy records m. 152-53° d[49e].

The residual oil was distilled in vacuum to give

1. b. 47-89°/0.5m.m. (6.3 g.), mostly boiled at 47-49°.
2. b. 94-114°/0.8 m.m. (14.3 g.).

The lower boiling fraction, shown by infra-red to be mixture of 1-bromo-2-chlorocyclohexane and 2-chlorocyclohexanol was combined with the corresponding fraction from the volatile fraction. The whole (16.4 g.) was treated with 85% phosphoric acid in an attempt to separate the alcohol. The phosphoric acid gave, on dilution, pure 2-chlorocyclohexanol (8.93 m. mole), identified by infra-red. The remainder of the fraction still contained alcohol [Infra-red. 3400 cm^{-1}, ν(O - H); 1080 cm^{-1}, ν(C - OH)] and the proportion of alcohol to chloro-bromide was therefore estimated quantitatively by infra-red spectrometry. This gave the weight % of 2-chlorocyclohexanol as 26.7%, and that of 1-bromo-2-chlorocyclohexane, independently, as 73.6%. Hence this fraction contains 2-chlorocyclohexanol (27.85 m. mole.) and 1-bromo-2-chlorocyclohexane (57.5 m. mole.). A portion of this mixture was

chromatographed in petroleum ether (b.40-60) on activated silica-gel, and gave pure 1-bromo-2-chloro-cyclohexane b.44°/0.6 m.m. (Found C, 36.23; H, 5.21; Cl, 17.80; Br, 40.12. On the assumption that the silver halide was a 1:1 mixture of chloride and bromide. Calc. for $C_6H_{10}BrCl$ C, 36.48; H, 5.10; Cl, 17.95; Br, 40.46%).

The higher boiling fraction was treated with 85% phosphoric acid and redistilled to give an oil (11.55 g.), which crystallised on cooling. By diluting with petroleum ether (b. 50-60°) and cooling, crystalline 2-bromo-1-nitrocyclohexane (20.2 m. mole.) was obtained. Colourless plates m. 38.5-39.5 after recrystallisation from petroleum ether (b. 60-80°) (Found: C, 35.05; H, 4.94; N, 6.60; Br, 38.18. $C_6H_{10}O_2NBr$ requires C, 34.63; H, 4.84; N, 6.73; Br, 38.41%). λ max 279 mμ, log ε 1.37; λ min 255 mμ (1.22). This is probably the trans isomer. A comparison of the infra-red spectrum of the residual oil with those of 2-bromo-1-nitrocyclohexane, 1-nitrocyclohexene and 2-chlorocyclohexyl nitrate showed that it consisted of a mixture of these three compounds and probably contained a little 1-bromo-2-chlorocyclohexane. Quantitative analysis by infra-red

spectrometry gave:

1-nitrocyclohexene	(1520 cm^{-1})	0.684mmole/g.
2-bromo-1-nitrocyclohexane	(1550 cm^{-1})	3.422 "
2-chlorocyclohexyl nitrate	(1643 cm^{-1})	0.850 "
1-bromo-2-chlorocyclohexane	(by difference)	0.246 ""

Carius analysis for total halogen fitted this result. (Found: 83.5% mixed silver halide. Calc. 84.6%).

Table IX gives the amounts of the various compounds detected.

TABLE IX

Compound		m.mole present
2-Bromo-1-nitrocyclohexane		56.15
2-Chlorocyclohexanol		52.1
2-Chlorocyclohexyl nitrate		7.74
1-Bromo-2-chlorocyclohexane		59.74
Trichloronitromethane	not less than	3.04
cycloHexene nitrosite	" " "	1.6
1-Nitrocyclohexene		6.2

% Recovery on cyclohexene = 63%; on N_2O_4 = 66%.

Dinitrogen tetroxide with cyclohexene

Dinitrogen tetroxide (331.5 m. mole) was distilled in a slow stream of oxygen, into cyclohexene (376 m. mole) in ether (350 ml.) at 0°C. The solvent was stripped off and the involatile products stirred (½ hr.) with warm water (200 ml.) and treated with urea until a negative starch-iodide test was obtained. The process was repeated 3 times with 100 ml. portions of water. The aqueous extracts were combined, neutralised to pH5 to 6 with bicarbonate and continuously extracted with ether for 80 hrs. The extract was evaporated and the resultant oil dried by adding benzene and distilling the water out azeotropically. Distillation under reduced pressure gave a mixture of the isomeric 2-nitrocyclohexanols b. 76-80°/0.1 m.m. (127.5 m. mole.; 38.5%).

The water-insoluble fraction was dried azeotropically and distilled to give

1. b. 40-93°/0.4 m.m. (5.2 g.) shown by infra-red to be mainly 1-nitrocyclohexene [40.9 m. mole., as 1-nitrocyclohexene; 12.3%].
2. b. 93-104°/0.4 m.m. (14.5 g.) shown by infra-red to be a mixture of 2-nitrocyclohexyl nitrate and 1:2-dinitrocyclohexane.
3. b. 105-120°/0.4 m.m. (10.1 g.) shown by infra-red to be mainly 1:2-dinitrocyclohexane with a little nitrate.

The mixture of epimeric 2-nitrocyclohexanols was fractionated in a column of 12 theoretical plates to give

1. b. 74.5-82°/1.0 to 1.3 m.m.
2. b. 81.5-84°/0.9 to 1.3 m.m.
3. b. 84.5-87°/1.4 to 1.5 m.m.
4. b. 87-88°/1.7 m.m.

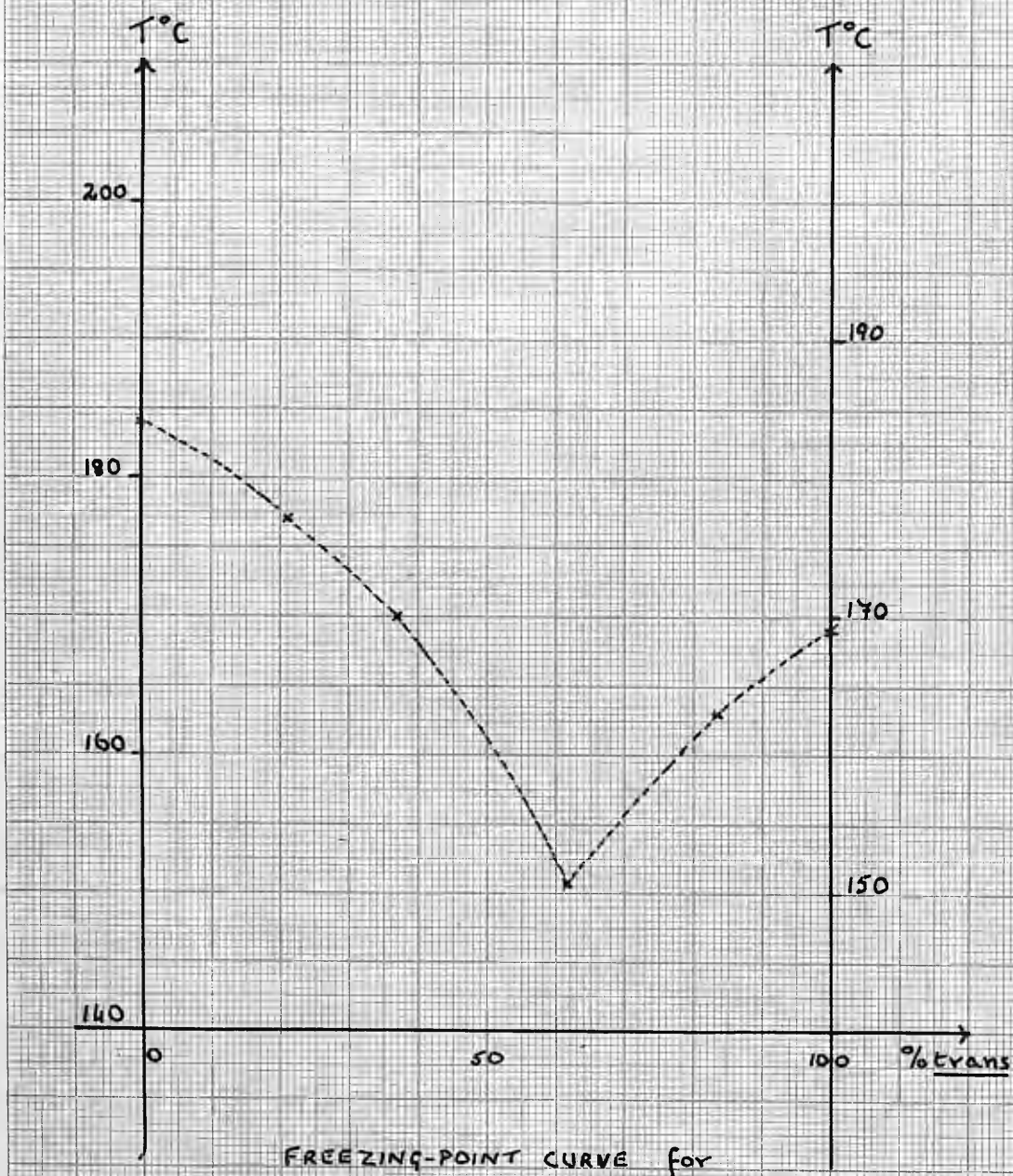
+ residue not distilled.

The residual oil crystallised on cooling, and fraction 4 did so after seeding. Recrystallisation from chloroform-petroleum ether (b. 60-80°) gave colourless needles of trans-2-nitrocyclohexanol, m. 46.5-47.5°. (Found: C, 49.74; H, 7.42; N, 9.57. Calc. for $C_6H_{11}O_3N$ C, 49.62; H, 7.64; N, 9.65%). λ max 279 mμ, log ε 1.54; λ min 255 mμ (1.29). A comparison of the infra-red spectrum of fraction 1 with that of the crystalline trans alcohol showed that it was the cis isomer.

Stereochemistry of the addition of dinitrogen tetroxide to cyclohexene

The reaction was carried out as above, but in order to minimise the formation of nitrate, which Levy had

shown to be favoured by oxygen[49a] a stream of nitrogen was bubbled through the reaction vessel as the N_2O_4 was distilled into it. N_2O_4 (158 m. mole) was reacted with cyclohexane (189 m. mole). After working up as above, the aqueous layers gave, after extraction and distillation, 2-nitrocyclohexanol (42.8 m. mole), which on cooling and seeding gave crystalline alcohol (7.59 m. mole). Of this crystalline 2-nitrocyclohexanol, 3.34 m. mole was reduced with palladised charcoal[54] and hydrogen. The uptake of hydrogen was theoretical in 2½ hrs. After removal of catalyst and solvent (ethanol), the crystalline amine was treated with dry hydrogen chloride in ether-chloroform solution. The amine hydrochloride was filtered off, washed with anhydrous acetone and dried. Benzoylation according to the method of Leffler and Adams[48], followed by recrystallisation from ethanol gave trans-2-benzoylaminocyclohexanol (2.56 m. mole.) m. 168-9°, undepressed on admixture with an authentic specimen prepared by the method of McCasland et al[51]. Of the oil remaining after the removal of the crystals, 6.88 m. mole was reduced as above, and the amine benzoylated to give 4.71 m. mole of N-benzoyl derivative. After fractional



FREEZING-POINT CURVE for

cis- and trans- 2-BENZOYLAMINOcyclo HEXANOL

crystallisation into 4 fractions, the cis-trans composition was determined by thermal analysis. Further crystallisation of the leading fraction gave pure cis-2-benzoylaminocyclohexanol m. 184-5° undepressed on admisture with a sample prepared by the method of McCasland et al[51].

Fraction	1	2	3	4
wt. (mg.)	360	50	283	297
m.p.	165-79-81	146-8-158	146-8-54	146-58-62
% trans	8	53	67	82
wt. trans (mg.)	28.8	26.5	189	243

Total wt. = 990 mg.

Total wt. trans = 487 mg.

Therefore cis:trans ratio in 2-nitrocyclohexanol as isolated from the reaction is 41.8:58.2.

A portion of the insoluble oil (dinitrocyclohexane fraction) from this experiment was chromatographed in benzene solution on activated silica-gel and a crystalline sample of 1:2-dinitrocyclohexane obtained. After recrystallisation from chloroform-

petroleum ether (b. 60-80°) this gave colourless needles of (probably trans) 1:2-dinitrocyclohexane m. 45-6° (Found C, 41.7; H, 5.5; N, 16.3. Calc. for $C_6H_{10}O_4N_2$ C, 41.4; H, 5.8; N, 16.1%). Attempts to establish the stereochemistry by catalytic hydrogenation to the diamine (trans isomer known)[83] were unsuccessful.

Test for isomerisation of 2-nitrocyclohexanol

trans-2-Nitrocyclohexanol (7.6 m. mole) m. 44-6° was dissolved in water (20 ml.) and added to 0.2 M nitrous acid solution (20 ml.). After 1½ hours, urea was added to destroy the nitrous acid, and after a further 20 hours, the solution was neutralised to pH5 to 6 with bicarbonate. It was then extracted with ether for 80 hrs., the extract evaporated and dried azeotropically. On complete removal of the benzene, the alcohol (6.9 m. mole.; 91%) crystallised, and had m. 43-6°, undepressed on admixture with starting material. Therefore no appreciable amount of isomerisation had taken place.

Dinitrogen tetroxide with 1-methylcyclohexene

Dinitrogen tetroxide (267.5 m. mole) was distilled in a slow stream of nitrogen into a solution of 1-methylcyclohexene (312.5 m. mole) in ether at -5°C. The dark blue reaction mixture was stripped and the product allowed to fall into urea (14 g.) in methanol (100 ml.) at -80°. The solution was allowed to warm to -4° overnight and the nitrosite (1.26 g.) filtered off. The methanol was removed under vacuum and the residual oil dissolved in benzene-petroleum ether (b.80-100) and extracted with water (10 x 20 ml.). The organic layer was evaporated under reduced pressure and gave a green oil (38.9 g.) which had bands in the infra-red at 1633 (w.) and 1290 (w.) due to small amounts of nitrate ester, and at 1550 (v.s.) and 1372 (s) due to an aliphatic nitro-group. A very weak band at 3480cm^{-1} showed that the fraction contained only a very small amount of alcohol. Distillation of a portion of this oil gave a pale yellow oil b. 110°/0.2 m.m., which solidified on cooling. Crystallisation from chloroform-cyclohexane gave needles m. 88-90°. Sublimation at 50°/0.05 m.m.

gave colourless 1-methyl-trans-1:2-dinitrocyclo-hexane m. 89-90.5°. (Found C, 44.76; H, 6.05; N, 14.65. $C_7H_{12}O_4N_2$ requires C, 44.68; H, 6.43; N, 14.88%). The stereo-chemistry was assigned by analogy with the corresponding alcohol (below), and on the stereo-specificity of the reaction.

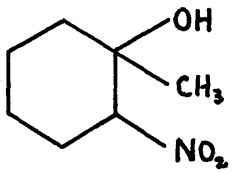
The aqueous extracts were neutralised to pH5 to 6 and extracted with chloroform (10 x 20 ml.). The extract was evaporated to dryness to give a pale green oil (6.03 g.) which crystallised. Recrystallisation from chloroform-cyclohexane gave pale yellow needles (3.34 g.), which were sublimed at 40-50°/0.02 m.m. giving colourless needles of 1-methyl-trans-2-nitro-cyclohexanol (3.26 g.) m. 71-2°, (Found C, 52.77; H, 7.89; N, 8.88. $C_7H_{13}O_3N$ requires C, 52.81; H, 8.23; N, 8.80%), λ max 282 mμ, log ε 1.82; λ min 257 mμ (1.57), and residue (80 mg.). The mother liquors were evaporated to dryness and sublimed to give 1-methyl-trans-2-nitrocyclohexanol (1.46 g.) (shown by infra-red to contain a little of a carboxylic acid) and residue (0.667 g.) - a mixture of alcohol and acid. Recovery (5.467 g.) was 91%. Of this 85% (4.66 g.) was pure 1-methyl-trans-2-nitrocyclo-hexanol, and the remainder was mainly an unidentified carboxylic acid plus involatile tars (infra-red);

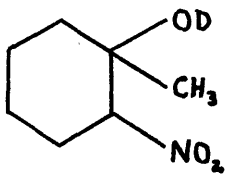
but see later.

1-Methyl-2-nitrocyclohexanol (200 mg.) m. 71-2° was catalytically hydrogenated, the catalyst removed, and dry hydrogen chloride passed. After evaporation to dryness, this gave amine hydrochloride (145 mg.; 70%) m. 160-161.5°, undepressed on admixture with a synthetic sample of 1-methyl-trans-2-amino-cyclohexanol hydrochloride. Benzoylation according to the method of Leffler and Adams[48] gave pure 1-methyl-trans-2-benzoylaminocyclohexanol m. 179-80°, undepressed when mixed with an authentic sample, and with an identical infra-red spectrum.

Distillation of the residue)0.667 g.) from the alcohol sublimation gave a pale yellow oil (0.34 g.) b. ca. 90°/0.1 m.m. and involatile tar (0.31 g.). Reduction of the distilled oil (175 mg.) gave, after working up, 1-methyl-trans-2-aminocyclohexanol hydrochloride (64 mg.; 35%) with infra-red spectrum identical with that of an authentic sample. There was no evidence for the presence of any other amine.

Deuteration of 1-methyl-trans-2-nitrocyclohexanol gave the O-deuterated alcohol. A comparison of its infra-red spectrum with that of the undeuterated alcohol showed that both existed as mixtures of the equatorial and axial conformational isomers.





ν (O-H)	3480	cm^{-1}	ν (O-D)	2605	cm^{-1}
ν (C - OH)(e)	992	cm^{-1}	ν (C-OD)(e)	994	"
(a)	928	cm^{-1}	(a)	929	"
ν (NO_2 as)	1542	"	ν (NO_2 as)	1542	"
ν (NO_2 s)	1367	"	ν (NO_2 s)	1367	"

Tracer deuteration experiments were also carried out to determine the number of hydrogen atoms exchangeable under acid conditions. 1-Methyl-trans-2-nitrocyclohexanol (192.3 mg.) was dissolved in methanol (11.8165 g.) and deuterium oxide (85.5 mg.) added. For solvent % D/D + H = 2.254%.

$\therefore$ % D/D + H in nitro-alcohol for 1 atom exchanged

= 0.1733%

for 2 atoms exchanged

= 0.3466%.

One small drop of conc. hydrochloric acid, sufficient to take the pH to 1 to 2, was added, and the solution

left at room temperature for ca. 18 hrs. The methanol was removed under vacuum, and the solid nitro-alcohol transferred to a combustion boat in a dry-box. The atom % of deuterium in the water produced by combustion was determined from the intensity of the HOD band at 2480 cm^{-1} in the infra-red.

Found Atom % deuterium = 0.244%

∴ Atoms hydrogen exchanged = 1.29.

Dinitrogen tetroxide with cyclopentene

Dinitrogen tetroxide (212 m. mole) was distilled in a slow current of oxygen into a solution of cyclopentene (235 m. mole) in ether at 0°. The reaction was worked up by stripping the products into methanolic urea solution (100 ml.) at -80°. The methanol was allowed to warm to -4°, overnight, and then removed under vacuum. Water (30 ml.) was added and the oil extracted with water (5 x 30 ml. + 20 x 10 ml.) The residual oil (13.48 g.) was shown, by infra-red spectrometry, still to contain a little alcohol [ν (O - H) 3400 cm^{-1}]; but was not worked up further. The aqueous extracts were neutralised to pH5 to 6 and extracted with methylene chloride (20 x 20 ml.).

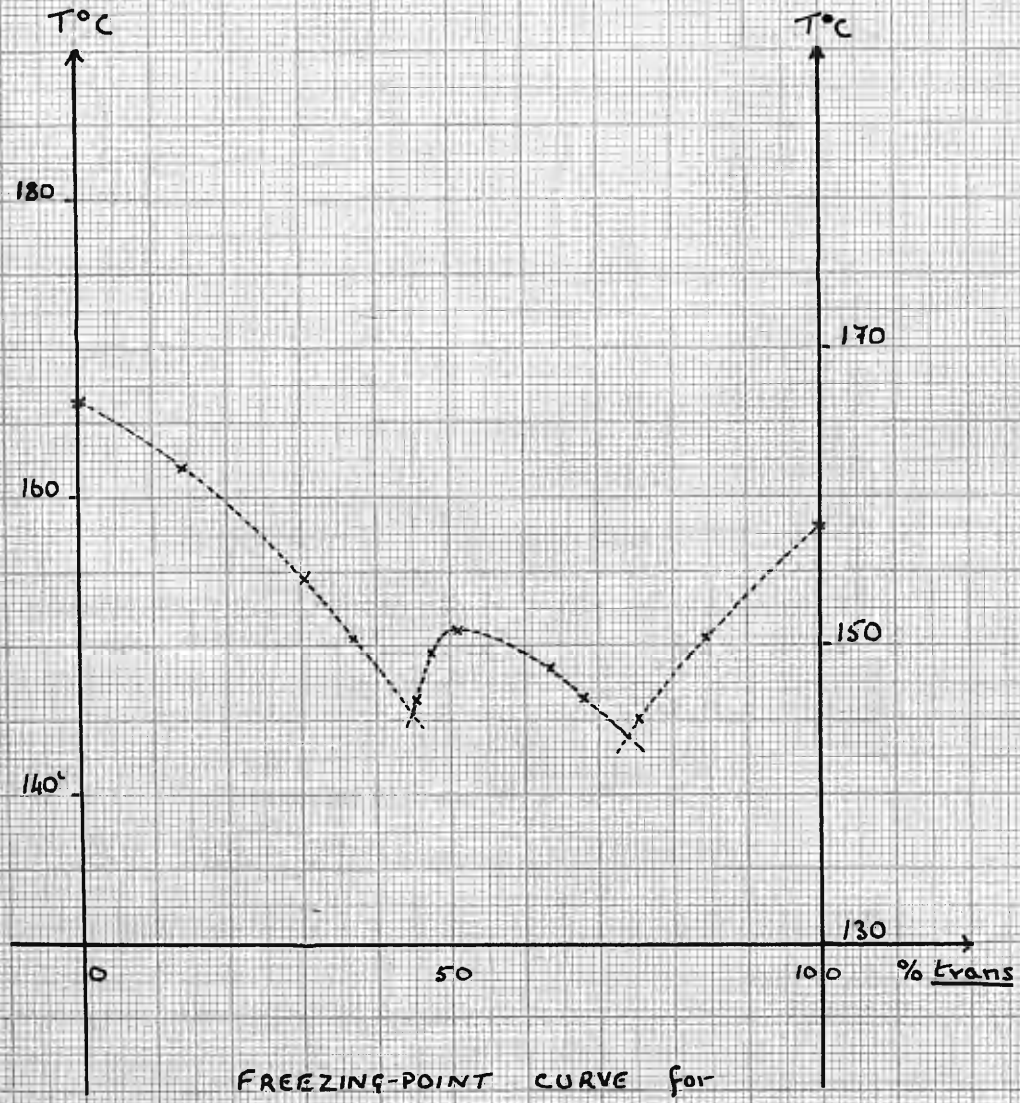
Evaporation gave a pale yellow oil (15.27 g.) shown by infra-red to contain appreciable quantities of a carboxylic acid. It was dissolved in benzene and extracted twice with 5% aqueous bicarbonate solution. Evaporation of the benzene layer gave an oil (13.03 g.) shown by infra-red to be mainly a nitro-alcohol. This oil was distilled under vacuum to give

1. b. 78-9°/0.25 m.m. (8.9 g.)

2. b. 79-82°/0.25 m.m. (1.23 g.)

3. Residue (2.9 g.) which underwent a low-order explosion on attempted distillation. The infra-red spectrum of the distilled alcohol showed only a very small band at 1706 cm^{-1} [ν (C = O)], together with strong bands at 3380 [ν (O - H)], 1550 [ν (NO_2 as)], 1374 [ν (NO_2 s)] and 1092 cm^{-1} [? δ (OH)] consistent with it being a nitro-alcohol.

The nitro-alcohol (9.7 m. mole) was reduced catalytically with palladium-charcoal and took up the theoretical volume of hydrogen. After removal of catalyst, dry hydrogen chloride was bubbled into the solution, and then the solvent (ethanol) evaporated to dryness. The amine hydrochloride (6.96 m. mole) was washed with acetone, dried and p-nitrobenzoylated by the method of Leffler and Adams[48], to give a



FREEZING-POINT CURVE for

cis- and trans-2-(p-NITROBENZOYLAMINO) cyclo PENTANOL

mixture of cis and trans-2-(p-nitrobenzoylamino)-cyclopentanols (5.43 m. mole). This mixture was fractionally crystallised into eight fractions, whose compositions were then determined by thermal analysis. Further crystallisation of the leading fraction gave trans-2-(p-nitrobenzoylamino)cyclohexanol m. 157-157.5°. McCasland and Smith give 160°[52].

Fraction	m °C.	wt.(mg.)	% trans	wt. trans
1.	154-157-157.5°	232	99	229.5
2.	140-156.5-157.5	195	98.5	192
3.	143-146.5-147.5	323	64	206.6
4.	140-155.5-156.5	227	96.5	218.8
5.	140-142	33	74	24.4
6.	143-147	119	79	94
7.	140-142	119	74	88
8.	140	47	74	34.8
		1,295		1,088.1

95% recovery. ∴ % trans = 84

Therefore, cis:trans ratio in isolated alcohol = 16:84.

To obtain cis-2-(p-nitrobenzoylamino)cyclopentanol for the freezing-point curve, some mainly trans-amino-alcohol was converted to the cis isomer by the

method of McCasland and Smith[52]. The (mainly) trans-2-(p-nitrobenzoylamino)cyclopentanol (1.4 g.) was treated with thionyl chloride (4 times excess) for 3 hrs. at 25°. The thionyl chloride was removed under vacuum and the resultant oil triturated with ether to give a crystalline solid. This solid was hydrolysed with dilute hydrochloric acid (2 hrs. at 100°), filtered and the filtrate evaporated to small bulk. Concentrated potassium hydroxide solution was added and the precipitated solid filtered (0.53 g.). Recrystallisation from aqueous alcohol gave needles of cis-2-(p-nitrobenzoylamino)cyclopentanol, m. 165-66°. McCasland and Smith give 167°[52].

Dinitrogen tetroxide with 3-methylcholest-2-ene

a. Oxygen present

Dinitrogen tetroxide (27.2 m. mole) was reacted with 3-methylcholest-2-ene (26.65 mole) in ether. Solvent was removed at 0° under reduced pressure to give a yellow semi-solid. The infra-red spectrum showed bands at 1633 and 1294 cm^{-1} [(ONO_2as) and (ONO_2s)] and at 1552 and 1366 cm^{-1} [(-NO_2as) and (NO_2s)]. The ultra-violet spectrum showed no evidence for any nitrite ester. Chromatography of a portion on

alumina lead to extensive decomposition. Chromatography on activated silica-gel showed that the main products were not readily separated, although a sample of 2-nitro-3-methylcholestan-3-yl nitrate was obtained pure m. 157-8° (after recrystallisation) (Found C, 68.31; H, 9.70; N, 5.80. $C_{28}H_{48}O_5N_2$ requires C, 68.26; H, 9.81; N, 5.69%). The remaining fractions all showed bands in the infra-red at 1518 and 1332 cm^{-1}, due to an α-β unsaturated nitro-group, showing that elimination had taken place.

b. Oxygen absent

Dinitrogen tetroxide (24.5 m. mole) was reacted with 3-methylcholest-2-ene (24.5 m. mole) with a slow stream of nitrogen passing through the reaction mixture. Removal of solvent gave a pale blue semi-solid which had infra-red absorbtion bands at 1655, 1118 and 1079 cm^{-1} [ν (N = O) of a nitrate ester and ν (C - ONO)], and at 1555 and 1368 cm^{-1} [ν (NO_2as) and ν (NO_2s)]. This solid was dissolved in benzene and a methanolic urea solution added to solvolyse the nitrite ester. Removal of solvent, followed by dissolution in benzene, filtration (to remove urea)

and evaporation to dryness gave a semi-solid with infra-red absorbtion bands at 3535cm^{-1} [ν (O - H], weak bands at 1637 and 1292 cm^{-1} (nitrate ester), and strong bands at 1555 and 1368 cm^{-1} (aliphatic nitro-group). This semi-solid was dissolved in petroleum ether (b. 40-60°) and a white solid was left behind. This solid was recrystallised from benzene-ethanol to give plates of 3-methylcholest-2-ene nitrosite m. 182-4°. (Found C, 72.05; H, 10.46. $C_{28}H_{48}O_3N_2$ requires C, 73.0; H, 10.50%).

The petroleum ether solution of products was chromatographed on activated silica-gel. 3-methylcholest-2-ene (6.62 m. mole) was recovered. Elution with benzene-petroleum ether (b. 40-60°) (1:1, v:v) gave successively (i) 3-methyl-2:3-dinitrocholestane (1.84 g.) contaminated with nitrate and unsaturated nitro-compound, (ii) a mixture (1.77 g.) of the dinitro-compound, the nitrate ester and 3-methyl-2-nitrocholest-2-ene, (iii) a mixture (1.1 g.) of the dinitro-compound and the unsaturated nitro-compound. Elution with chloroform-benzene (1:4, v:v) gave nitro-alcohol (0.76 g.), followed by a further 1.93 g. Both the alcohol fractions were contaminated with unsaturated nitro-compound. The first alcohol fraction was

recrystallised from petroleum ether (b. 40-60°) - benzene to give colourless plates of 3-methyl-2-nitrocholestan-3-ol m. 130-2°. (Found C, 75.30; H, 11.37; N, 3.45. $C_{28}H_{49}O_3N$ requires C, 75.12; H, 11.03; N, 3.13%).

Control experiments showed that the nitro-alcohol was dehydrated, though not quantitatively by silica-gel.

A separation which gave substantially pure nitro-alcohol, without decomposition, free from dinitro-compound and nitro-nitrate ester was achieved by countercurrent distribution between iso-octane (2:2:4-trimethyl-pentane) and β-methoxy-ethanol in a 50 transfer Craig machine. The first 25 tubes of either phase contained material shown by infra-red to be nitro-alcohol. Attempted hydrogenation of this material with palladium-charcoal or Adams' platinum oxide catalysts gave only unchanged starting material.

Nitryl chloride with cyclohexene

Nitryl chloride (295 m. mole) was distilled in a stream of oxygen into a solution of cyclohexene (324 m. mole) in dry ether (300 ml.) at 0°. Solvent was stripped from the blue reaction mixture in the

film evaporator, and the oily product allowed to fall into water. The white solid (3.96 g.), which had precipitated during the reaction, was filtered off and the oil dissolved in pentane (50 ml.) and extracted with water (5 x 50 ml. + 25 x 25 ml. + 25 x 15 ml.), sufficient urea being added to decompose any nitrous acid formed. The residual water-insoluble oil (29.9 g.) was dried azeotropically and the components (1:2-dichlorocyclohexane, 2-chloro-1-nitrocyclohexane and 2-chlorocyclohexyl nitrate) estimated by analysis in the infra-red absorbtion spectrum. The results are recorded below. Distillation of a portion of this mixture gave a fraction b. 78-85°/15 m.m., which was dissolved in petroleum ether (b. 40-60°) and filtered through activated silica-gel to give trans-1:2-dichlorocyclohexane b. 78-9°/18 m.m. n_D^{19} 1.4904. Stevens and Grummitt report b. 88-9/30 m.m., n_D^{20} 1.4904[76]. Carroll et al. report b. 71.1°/15m.m., n_D^{20} 1.4902[21], whose infra-red absorbtion spectrum showed no traces of absorbtion due to the cis isomer[76].

The white solid was not positively identified, but was apparently a mixture of the dimeric

1-chloro-2-nitroso- and 1-nitro-2-nitrosocyclohexanes. (Sodium fusion showed N and Cl, a blue colour was formed reversibly on heating in solution and oxides of nitrogen were evolved on melting). Carius analysis gave 6.1% of chlorine, and on this basis the mixture was taken to be 1-chloro-2-nitrosocyclohexane (6.82 m. mole) and 1-nitro-2-nitrosocyclohexane (cyclohexene nitrosite) (18.7 m. mole).

The aqueous extracts were re-extracted with ether for 80 hrs., and the oil obtained distilled through a 4" Vigreux column to give (i) b. 68-76°/12 m.m. (2.6 g.).

(ii)b. 76-80°/12 m.m. (0.45g.)

(iii)b. 78-84°/0.25m.m.(1.7 g.)

Fraction (i) was shown by infra-red to be a mixture of cyclohexen-3-ol and 2-chlorocyclohexanol. Carius estimation of chlorine gave 19.7% chlorine, equivalent to 74% of 2-chlorocyclohexanol (by weight). This was in fair agreement with an analysis for cyclohexen-3-ol based on infra-red of 30% (by weight). Careful fractionation of this fraction in a column of 12 theoretical plates gave

(iv) b. 64-66°/11 m.m. cyclohexen-3-ol. Phenyl urethane m. 106-7° (Found C, 72.10; H, 7.20. Calc. for $C_{13}H_{15}O_2N$, C, 71.86; H, 6.96%), α-naphthyl

urethane m. 155° (Found C, 76.6; H, 5.96. Calc. for $C_{17}H_{17}O_2N$, C, 76.38; H, 6.41%). Clarke and Owen give for cyclohexen-3-ol b. 64-5°/12 m.m., phenyl urethane m. 107°, α-naphthyl urethane m. 155°[22]. (v) b. 78-80°/12 m.m. a mixture of cis and trans-2-chlorocyclohexanols.

Fraction (ii) was shown by infra-red to be a mixture of 2-chlorocyclohexanol (1.67 m. mole) and 2-nitrocyclohexanol (1.55 m. mole). Fraction (iii) was identified as 2-nitrocyclohexanol (11.7 m. mole).

TABLE X

Compound	m. mole present
2-chloro-1-nitrocyclohexane	102
1:2-dichlorocyclohexane	65.2
2-chlorocyclohexyl nitrate	15.6
2-chlorocyclohexanol	16.0
2-nitrocyclohexanol	13.25
1-chloro-2-nitrosocyclohexane	6.8
1-nitro-2-nitrosocyclohexane	18.7
cyclohexen-3-ol	6.9

Total = 244.45 m. mole.

∴ Yield = 83% on nitryl chloride.

The stereochemistry of the 2-chlorocyclohexanol fraction and of the 2-nitrocyclohexanol fraction was determined by infra-red spectrometry.

	band(cm^{-1})	% cis	% trans
2-chlorocyclohexanol	809	38.6	-
	796	-	62.3
2-nitrocyclohexanol	862	-	62.3

The cis-2-chlorocyclohexanol for comparison purposes was prepared by the method of Bartlett[5], and the trans isomer by the method of 'Organic Syntheses'[23].

Reference Compounds

1-Bromo-2-chlorocyclohexane

This was prepared according to the general method of Ziegler and Shabica[81]. cf. also Goering and Sims[33].

A slurry of N-bromosuccinimide (280 m. mole) in chloroform (60 ml.) was added in portions to a stirred solution of cyclohexene (300 m. mole) in chloroform (120 ml.) while dry hydrogen chloride was passed into the solution through a gas delivery tube fitted with a sintered-glass disk. After addition was complete, the succinimide was filtered off and the organic layer washed with water and 10% aqueous sodium carbonate, and dried ($MgSO_4$). The chloroform was distilled off, and the residual oil examined by infra-red. This showed it to contain an alcoholic impurity, and it was therefore extracted with 85% phosphoric acid, washed with water, dried and distilled to give a colourless oil (31.2 g.) b. 90-91°/17 m.m., n_D^{20} 1.5181, m. -22.5 to -21°. This was still contaminated by the alcoholic impurity, and so a portion was dissolved in petroleum ether (b. 40-60°) and filtered through activated silica-gel. Distillation gave pure 1-bromo-2-chlorocyclohexane b. 59-60°/2.5 m.m., n_D^{21} 1.5203, m -11.5 to -11°. As

these constants lie between those reported by Goering and Sims for the cis and trans isomers, this sample is obviously a mixture.

Goering and Sims record[33].

cis	trans
b. 87.5-88°/7 m.m.	76.5-77°/9 m.m.
n_D^{25} 1.5238	1.5173
m. -7.5 to -5.5°	-19.5 to -18°

trans-2-Chlorocyclohexyl nitrate

This preparation was based on the two reactions.

$$R - OH + N_2O_4 \longrightarrow RONO + HNO_3 \quad ^{36}$$

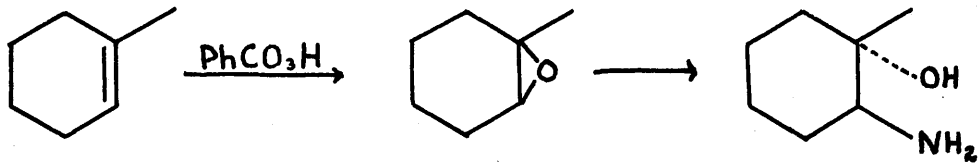
$$R.ONO + N_2O_5 \longrightarrow RONO_2 + N_2O_4 \quad ^{12b}$$

trans-2-Chlorocyclohexanol (65.3 m. mole), prepared as in 'Organic Syntheses,'[23] in dry ether was esterified by distilling dinitrogen tetroxide (67.4 m. mole) into the solution. The nitrite ester was oxidised, without isolation, by then distilling

dinitrogen pentoxide into the solution. Aqueous sodium bicarbonate was added, to neutralise the nitric acid, and the ether layer washed and dried. Removal of the solvent gave an oil which was washed with 85% phosphoric acid and distilled to give trans-2-chlorocyclohexyl nitrate (4.97 m. mole) (4.97 m. mole) b. 88-9°/5 m.m. n_D^{16} 1.4830. (Found C, 40.42; H, 5.60. $C_6H_{10}O_3NCl$ requires C, 40.12; H, 5.61%).

1-Methyltrans-2-aminocyclohexanol

This was prepared by ammonolysis of 1-methyl-1:2-epoxycyclohexane[53].



To 1-methylcyclohexene (100 m. mole), in chloroform solution, was added a slight excess of perbenzoic acid, prepared by the method of 'Organic Syntheses,' [13] in chloroform at 0 to 10°. After 2 hrs. the reaction was complete, and the chloroform was distilled off and

the residual oil fractionated to give 1-methyl-1:2-epoxycyclohexane (63 m. mole) b. 136-9° n_D^{16} 1.4452. Boëseken records b. 137.9-138.3°/755 m.m., $n_D^{18.5}$ 1.4441 [11]. Of this 1-methyl-1:2-epoxycyclohexane (37.5 m. mole) and ammonia (S.G. 0.88; 25 ml.) were heated in a sealed tube at 108° for 6 hrs. The resulting solution was extracted with chloroform (15 x 15 ml.). Evaporation to dryness gave 4.92 g. of crude amine m. 88-91°. This was dissolved in chloroform-ether solution and treated with dry hydrogen chloride. The amine hydrochloride was filtered off and washed with anhydrous acetone to give 1-methyl-trans-2-amino-cyclohexanol hydrochloride m. 156-7° (33 m. moles.; 88%). Mousseron and Granger record amine m. 89-90°, hydrochloride m. 148-9° [53].

The above hydrochloride (5 m. mole) was benzoylated by the method of Leffler and Adams to give 1-methyl-trans 2-benzoylaminocyclohexanol (4.05 m. mole) m. 179-180°. (Found C, 72.24; H, 8.16. $C_{14}H_{19}O_2N$ requires C, 72.07; H, 8.21%).

1-Nitrocyclohexene

1:2-Dinitrocyclohexane (20 g.) was shaken with

sodium hydroxide (5.2 g) in water (100 m.l.) for 3 hrs. The oil was separated, the aqueous phase neutralised with acetic acid and extracted with ether. The whole of the oil was steam-distilled, the distillate extracted with ether, dried, evaporated and the residual oil fractionated to give 1-nitrocyclohexene (6.9 g.) b. 88-9°/7 m.m. n_D^{18} 1.5071, λ max 257 mμ, log ε 3.74; inflexion at λ 322 mμ (2.05). (Found C, 56.89; H, 6.80; N, 10.84. Calc. for $C_6H_9O_2N$ C, 56.68; H, 7.14; N, 11.02%). Levy et al.[49e] give b. 64°/ 1 m.m. Bloomfield and Jeffrey[82] record λ max 250 mμ, log ε 3.75; inflexion at λ 320 mμ (1.95).

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APPENDIX

Infra-red Spectra of Reference Compounds

Where bands are assigned to particular vibrations of functional groups, this has been done on the basis of the generalities discussed by Bellamy[10], Brown[15], and Kornblum et.al.[47].

Except where indicated, all spectra refer to capillary films. Bands marked s are strong bands and those marked w are weak ones; where no indication is given the bands are of medium intensity. Bands marked † were used for quantitative analysis. The positions of bands are given in cm^{-1}. The bands near 2900, 2800 and 1450cm^{-1}, due to the C-H stretching and deformation vibrations and common to all cyclohexane derivatives, are omitted.

Nitryl Chloride			Trichloronitromethane	
(gas)[61]	(CCl_4)		(CCl_3Br)	
1685 s	1665 s	$\nu(NO_2)$as	1603 v.s.	$\nu(NO_2)$as
1318	1312		1365	
1293 s	1262 s	$\nu(NO_2)$s	1315 s	$\nu(NO_2)$s
794	809 w		1287	
			900 s	
			860 s	
			842 s	

cyclo<u>Hexane</u>-trans-1:2-<u>diol</u>

(Nujol)

3300	s	ν(OH)
1354		
1293		
1075	s	
1045	s	
930		
858		
680	(v. broad)	

cyclo<u>Hexen</u>-3-<u>ol</u>

3330	s	ν(OH)
3010		$\nu(=C\langle_{H})$
1647		ν(C=C)
1284		
1069	s	ν(C-OH)
1053		
960	s	
896		
805		
727	s	(CCl)

trans-2-<u>Nitro</u>cyclo<u>hexanol</u>

	($CHCl_3$)		
	3560		ν(OH)
3350	3415		
1552	s 1552	v.s	$\nu(NO_2)$<u>as</u>
1376	1400	s	ν " <u>s</u>
1242	1238		
1070	s 1080	s	ν(C-OH)<u>e</u>
975	980		ν(C-OH)<u>a</u>
	958		
894	897	w	
862	862		

cis-2-<u>Nitro</u>cyclo<u>hexanol</u>

($CHCl_3$)			
3560			ν(OH)
3415			
1552	v.s		$\nu(NO_2)$<u>as</u>
1400	s		ν " <u>s</u>
1230			
1086			ν(C-OH)<u>e</u>
1010			
980	s		ν(C-OH)<u>a</u>
923			
888			
847	w		
827			

trans-1:2-Dinitrocyclohexane				1-Methyl-trans-1:2-dinitrocyclohexane			
		($CHCl_3$)		(Nujol)		(CHCl₃)	
1560	v.s.	1568	v.s. $\nu(NO_2)$as	1556	s.	1568	s $\nu(NO_2)$as
		1557		1550		1553	
1382	s.	1388	ν " s	1401		1396	δ(CH)in C-Me
1335		1336		1380	s.	1375	s $\nu(NO_2)$s
1284		1288		1361		1360	
1132		1140		1334		1333	
904		910		1319			
754				882		883	
740				763			
				684			

1-Methyl-trans-2-nitrocyclohexanol						
(Nujol)		($CHCl_3$;OH)		($CHCl_3$;OD)		
3295	s	3480				ν(OH)
3240		3368				
				2605		ν(OD)
1550	s	1545	s	1542	s	$\nu(NO_2)$as
1390		1380		1382		δ(CH) in C-Me
1340	s	1366	s	1367	s	$\nu(NO_2)$s
		1226		1220		
1170						
		1154		1154		
1129		1130				δ(OH)e
		1118		1118		
1010		1062				δ(OH)a
1001		992		994		ν(C-OH), ν(C-OD)e
		928		929		ν(C-OH), ν(C-OD)a
867		862		862		
741						

1-Methyl-trans-2-benzoylaminocyclohexanol

(Nujol)

3385	ν(OH)	1242		
3270	ν(NH)	1154		
1640 s	Amide I	989	ν (C-OH)e	
1550 s	Amide II	925	ν(C-OH)a	
1332		840		
1289		696 s	Aromatic	δ (CH)

3-Methyl-2-nitro-cholestan-3-yl-nitrate

(KCl disc)

1630 s	$\nu(ONO_2)$as
1555 s	$\nu(NO_2)$as
1380	δ(CH)in C-Me
1364	$\nu(NO_2)$s
1296 s	$\nu(ONO_2)$s
1282 s	
1254	
861 s	(ONO_2)
841	

3-Methyl-2-nitro-cholestan-3-ol

(Florube)	(Nujol)	
3470	3470	ν(OH)
1545 s	1545 s	$\nu(NO_2)$as
1370 s		$\nu(NO_2)$s
	1124	
	956	
	858	
	772	
	733	

trans-1:2-Dichlorocyclohexane (CS_2)[76] see also Table V		cis-1:2-Dichlorocyclohexane (CS_2)[76]	
1227		1242	
1010			
985		990 s	
917 s		909 s	
		889+s	
870			
847		840	
833			
823		820	
749 s	ν (C-Cl)e	746 s	ν(C-Cl)e
741			
702	ν (C-Cl)a	702	ν(C-Cl)a

trans-2-Chlorocyclohexanol (CS_2) see also Table II		cis-2-Chlorocyclohexanol (CS_2)	
3540	ν (OH)	3530	ν (OH)
1272			
1224		1220	
1212			
1081 s	ν (C-OH)	1080 s	ν (C-OH)
1038		1071	
		991	
959		973	
796†		809†	
732	ν (C-Cl)e	731	ν(C-Cl)e
		689†w	ν(C-Cl)a

All the spectra reported were recorded on a Perkin-Elmer Model 13 Infra-red Spectrometer equipped with a sodium chloride optical system.